UNIVERSITY OF ZAGREB

SCHOOL OF MEDICINE

Alma Biščević

Prospective comparison of two excimer laser platforms in treatment of high astigmatism with laser in situ keratomileusis

DISSERTATION

Zagreb, 2019.

UNIVERSITY OF ZAGREB

SCHOOL OF MEDICINE

Alma Biščević

Prospective comparison of two excimer laser platforms in treatment of high astigmatism with laser in situ keratomileusis

DISSERTATION

Zagreb, 2019.

Dissertation was fully conducted at University Eye Hospital Svjetlost Zagreb, School of Medicine, University of Rijeka.

Mentor: Prof. Iva Dekaris, MD, PhD

THANK YOU NOTE

I would like to thank my mentor Prof. Iva Dekaris, MD, PhD, and Prof. Nikica Gabrić MD, PhD, for the help in the study design and conception, together with continuous help and support during conduction of the study. Also, I would like to give special thanks to my co-worker and friend Maja Bohac, MD, PhD, for the help in study conduction and critical evaluation of the data and final work. In addition, I would like to say thank you to my colleague Mateja Končarević, MD, for the help in patient selection and data collection and Prof. Sudi Patel, PhD, for helping with the statistical part of the thesis.

I would like to give special thanks to University Eye Hospital Svjetlost in Zagreb for financial help during my years of PhD studies and also during the complete research and conduction of this study.

And finally, special thanks to my parents, for all the love and support...

CONTENTS:

LIST OF ABBREVIATIONS:

mm .... millimeter
D .... diopter
3-D .... three dimensional
% .... percent
RGP .... rigid gas permeable contact lenses
RK .... radial keratotomy
AK .... arcuate keratotomy
ARC-T .... astigmatism reduction clinical trial
LRI .... limbal relaxing incision
UDVA .... uncorrected distance visual acuity
ICR .... intrastromal corneal rings
FS .... femtosecond
PMMA .... polymethylmethacrylate
PRK .... photorefractive keratotomy
T-PRK .... trans-photorefractive keratotomy
LASIK .... Laser in situ keratomileusis
BKS .... Barraquer-Krumeich-Swinger
μm .... micrometer
IOL .... intraocular lens
pIOL .... phakic intraocular lens
s .... second
nm .... nanometer
SMILE .... small incision lenticule extraction
ReLex Flex .... refractive lenticule extraction
UV-C .... short-wavelength UV
ns .... nanosecond
Hz .... hertz
mJ .... millijoule
cm^2 .... square centimeter
WF .... wavefront
HOAs .... high order aberrations
RMS .... root mean square
APV .... astigmatic power vector
J .... Jackson crossed cylinder
TIA .... target induced astigmatism
SIA .... surgically induced astigmatism
DV .... difference vector
SA .... spherical aberration

1. INTRODUCTION

Humans have developed systems for detecting changes in the external environment. The known senses are: sight (ophthalmoception), taste (gustaoception), smell (olfacception) and touch (tactioception). We perceive up to 80 percent of all impressions by means of our sight so by far the most important organs of sense are our eyes. If other senses stop working, it's the eyes that best protect us from danger. Vision occurs when light is processed by the eye, and then interpreted by the brain.

1.1. ANATOMY OF THE EYE

First transparent eye surface responsible for vision is cornea.

The cornea is a transparent avascular tissue with a smooth, convex outer surface and concave inner surface, of which the main function is optical. The axial thickness of the cornea ranges from 0.50 to 0.52 millimeters (mm), with 5 histological layers. [1-3]

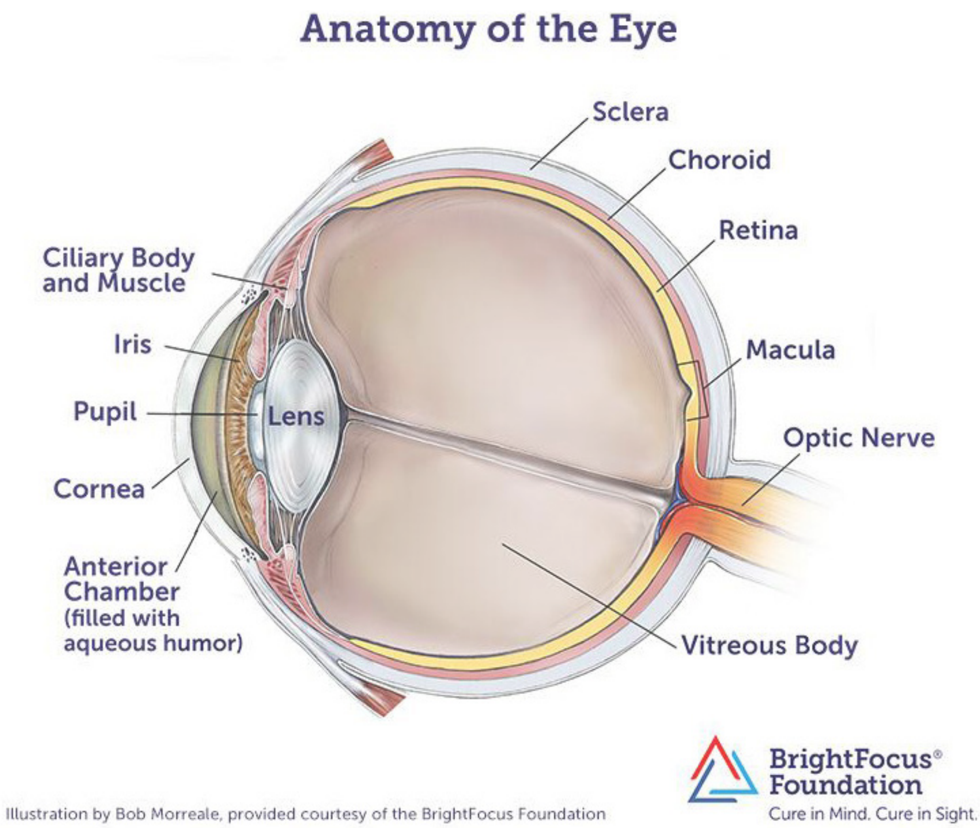
The epithelium, the outermost layer (1st layer), provides a smooth refractive surface and serves as a barrier against microorganisms. Bowman's layer (2nd layer) is a narrow, acellular, homogeneous zone with uncertain functions. The resistance of the cornea is due to the collagenous components of the stroma (3rd layer), accounting for 90% of the corneal thickness. [4-6]

The endothelium and its basement membrane (Descemet's membrane, the 4th layer) are responsible for the relative dehydration necessary for corneal clarity via an active sodium potassium – adenosine triphosphatase pump. [7]

Cornea, anterior chamber and lens refract light, with the cornea accounting for approximately two-thirds of the eye's total optical power. In humans, the refractive power of the cornea is approximately 43 diopters (D). [8]

When the light passes through the cornea, it goes through the pupil that is controlled by the iris and then it passes through flexible crystaline lens that focuses light on the retina. On the way to the retina light also passes through the interior of the eye that is filled with gel fluid called corpus vitreous. Retina converts the light into nerve impulses which are carried with neurons to the vision centers in the brain and there they get interpreted so we can see.

FIGURE 1. Anatomy of the eye



1.2. ASTIGMATISM

1.2.1. HISTORICAL BACKGROUND

Sir Isaac Newton was one of the first scientists who considered question of astigmatism in the late 1727. In 1801, the scientist Thomas Young continued investigation of astigmatism in details and was the first one to report it. [9]

In 1827 Cambridge astronomer Airy first corrected astigmatism with a cylindrical lens. However, the invention of the keratometer by Helmholtz in 1856 and the work of Donders in 1864, "Astigmatism and Cylindrical Lenses" brought astigmatism on the map as something of importance. Donders was probably the first to include cylinder lenses in the trial case for refraction. In 1869 Snellen made early attempts in surgical correction of astigmatism. His theories and theories of Bates (1891), Luciola (1893) and Dognoff (1895) were confirmed by Lans in 1897. [10]

1.2.2. DEFINITION AND CLASSIFICATION OF ASTIGMATISM

Astigmatism is a type of refractive error in which the eye does not focus light evenly on the retina. [11]

When the light is not evenly focused on the retina picture that we are seeing is going to be blurred and vision is poor. Another common symptom is the streak phenomena of rays around point sources of light, most noticeable in dark environments. If the amount of astigmatism is high, it may induce letters to have shadows or smear around it and in very high amounts, it may cause diplopia.

FIGURE 2. Astigmatism image

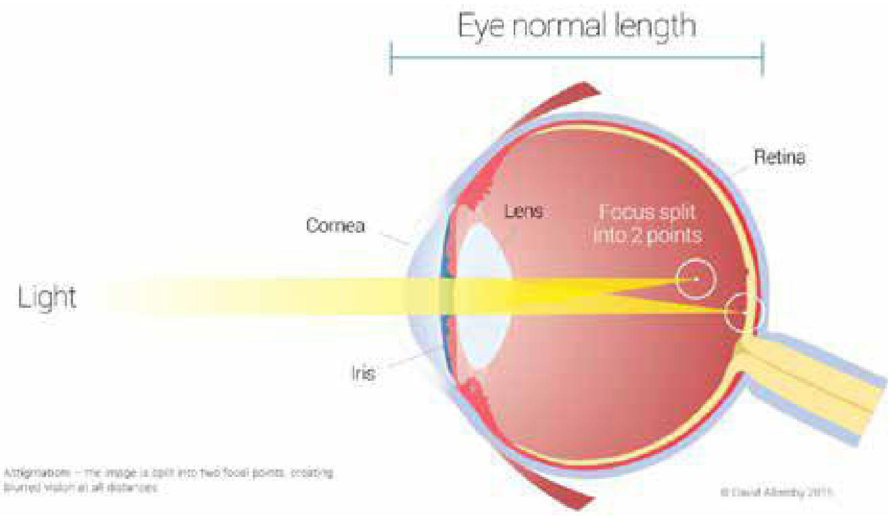


Illustration courtesy by © David Allamby 2015

FIGURE 3. Cross section of astigmatic eye

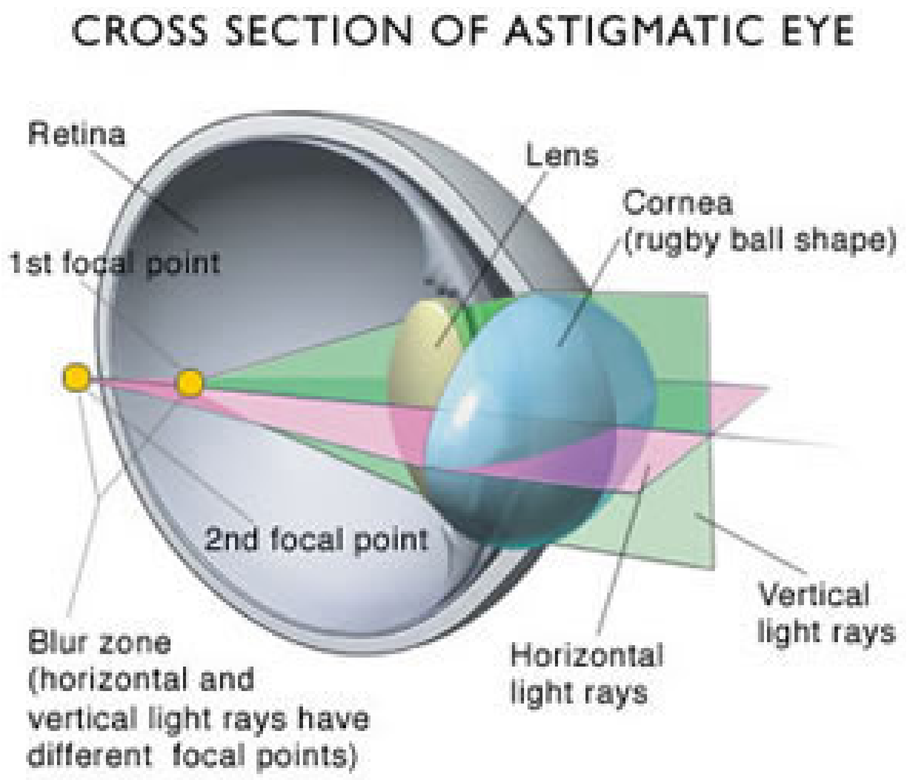


Illustration courtesy Ciba Vision®

The total amount of astigmatism is entirely dependent upon the anatomy of the eye. All segments of the physical optical media, including the cornea, the lens, and even occasionally the retina, can contribute toward the development of astigmatism, and each should be examined to understand its role in relation to the disorder.

The prevalence of astigmatism greater than 1 D in the general population is reported to be between 32% and 56%. [12, 13]

It is known that higher degrees of astigmatism are more common in eyes with a higher level of ametropia. [14-16]

In most cases, astigmatism is a result of the corneal shape (and sometimes the lens) that is present since birth. Normally, the surface of the cornea is rounded, however in astigmatism the cornea is shaped more oval. In eyes without astigmatism, the cornea and lens have a more or less similar curvature in all directions. This allows light to be focused to a single point on the retina.

In astigmatism the cornea is elliptically shaped. There is a long meridian and a short meridian. These two meridians generally have a constant curvature and are generally perpendicular to each other (regular astigmatism). Irregular astigmatism may have more than two meridians of focus and they may not be 90° apart. A point of light, therefore, going through an astigmatic cornea will have two points of focus, instead of one nice sharp image on the retina. This will cause the person to have blurry vision. What the blur looks like will depend upon the amount and the direction of the astigmatism.

Lenticular astigmatism is similar to corneal astigmatism, except it exists in the lens rather than the cornea. The lens may have variations in its curvature rather than having a perfect curve, causing images to reach the back of the eye (the retina) imperfectly. Most people with lenticular astigmatism have a normal-shaped cornea and the defect is only in the curvature of the lens.

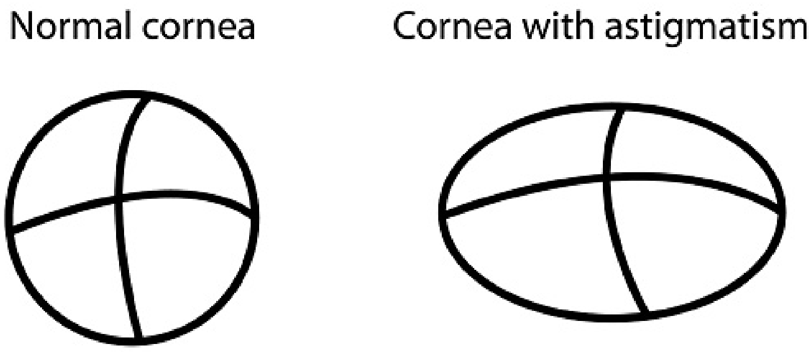
Astigmatism could be also related with retinal structure. Directional variability in photoreceptor arrangement was also proposed as a source of astigmatism. [17]

In other words, functional retinal elements may be more abundant or thicker in one axis than the other. [18]

In 1995 a “tilted” retina was simulated and it was observed to manifest as some degree of cylindrical error. [19]

This could be the result of unequal lengthening of the sclera in different meridians during axial growth. [20]

FIGURE 4. Image of normal and cornea with astigmatism



Source: National Eye Institute

There are different types of astigmatism. Depending on the axis of the principal meridian astigmatism can be:

- Regular astigmatism – principal meridians are perpendicular.
  - With-the-rule astigmatism – the vertical meridian is steepest (a rugby ball or American football lying on its side). [21]
  - Against-the-rule astigmatism – the horizontal meridian is steepest (a rugby ball or American football standing on its end). [21]
  - Oblique astigmatism – the steepest curve lies in between 120 and 150 degrees and 30 and 60 degrees. [21]
  - Irregular astigmatism – principal meridians are not perpendicular. [21]

In with-the-rule astigmatism, a minus cylinder is placed in the horizontal axis to correct the refractive error (or a plus cylinder in the vertical axis). Adding a minus cylinder in the horizontal axis makes the horizontal axis "steeper" (or better: makes the vertical axis "less steep") which makes both axes equally "steep". In against-the-rule astigmatism, a plus cylinder is added in the horizontal axis (or a minus cylinder in the vertical axis).

Axis is always recorded as an angle in degrees, between 0 and 180 degrees in a counter-clockwise direction. Both 0 and 180 degrees lie on a horizontal line at the level of the center of the pupil, and as seen by an observer, 0 lies on the right of both the eyes.

With accommodation relaxed, astigmatism can be:

- Simple astigmatism [21]
  - Simple hyperopic astigmatism – first focal line is on retina, while the second is located behind the retina.
  - Simple myopic astigmatism – first focal line is in front of the retina, while the second is on the retina.

- Compound astigmatism [21]
  - Compound hyperopic astigmatism – both focal lines are located behind the retina.
  - Compound myopic astigmatism – both focal lines are located in front of the retina.

- Mixed astigmatism – focal lines are on both sides of the retina (straddling the retina). [21]

There are certain eye conditions which are associated with astigmatism. Astigmatism can result from anomalies in corneal structure (e.g. corneal ecstasies and dystrophies). Some of the disorders are present from birth and some others develop throughout the life. The most common of these conditions is keratoconus. The prevalence of astigmatism is especially high in Down syndrome. [22]

In addition, astigmatism can result from an injury, scar or operation to the eye, particularly if the corneal surface is damaged. It can also result from anything pressing persistently on the surface of the cornea (such as a large lump on the eyelid) which pushes it out of shape.

1.2.3. ABERRATIONS OF THE EYE

Eye is not a perfect optical system; however, its imperfections cancel each other out through certain parts and in some other cases are adding to each other. An optical aberration is an imperfection in the image formation of an optical system. To understand that optical system we use Zernike polynomial expansion. [23-25]

Aberrations are alterations of the optical surfaces of the eye that lead to deviations in the light entering the eye, [26] causing a decline in visual quality and a loss of contrast sensitivity. [27]

Low order aberrations include myopia (positive defocus), hyperopia (negative defocus), and regular astigmatism. Other lower-order aberrations are non-visually significant aberrations known as first order aberrations, such as prisms and zero-order aberrations (piston). Low order aberrations account for approximately 90% of the overall wave aberrations in the eye. [28, 29]

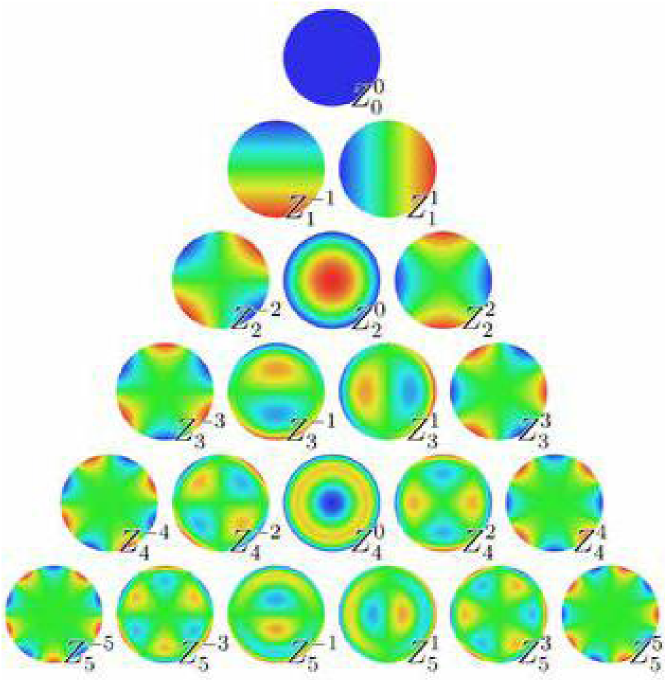
Higher-order aberrations comprise many varieties of aberrations. Some of them have names such as spherical aberration, coma and trefoil, but many more of them are identified only by mathematical expressions (Zernike polynomials). They make up about 10% of the total number of aberrations in an eye.

Spherical aberration results in halos around point images. Spherical aberration is defined as a second order aberration. Spherical aberration exacerbates myopia in low light (night myopia). In brighter conditions, the pupil constricts, blocking the more peripheral rays and minimizing the effect of spherical aberration. As the pupil enlarges, more peripheral rays enter the eye and the focus shifts anteriorly, making the patient slightly more myopic in low-light conditions. [28]

Coma causes light to be smeared like the tail of a comet in the night sky. Coma is defined as third order aberration and we have horizontal and vertical coma (axial and off-axis). Symptom of coma is usually double vision.

Trefoil (or elliptical coma) causes a point of light to smear in three dimensions and produces less degradation in image quality compared with coma. [29]

FIGURE 5. Image of Zernike polynomials



This chart reveals more common shapes of aberrations created when a wavefront of light passes through eyes with imperfect vision. A theoretically perfect eye (top) is represented by an aberration-free flat plane known, for reference, as piston. (Image: Alcon Inc.)

Today, it is possible to objectively evaluate the eye's optical quality in clinical practice using aberrometers, usually based on the Hartmann-Shack wavefront sensor [26, 30] or laser ray tracing [31, 32] and newer devices based on the double-pass technique. [33, 34]

Higher amounts of aberrations are primarily connected with irregular astigmatism.

1.3. ASTIGMATISM DIAGNOSTICS

1.3.1. KERATOMETERS

Keratometry is the measurement of the anterior corneal curvature and is traditionally performed with a manual keratometer. This device was developed by von Helmholtz in 1880. It is an instrument that gives 2 corneal curvature values (maximum and minimum) 90 degrees apart.

The two basic keratometers are the Helmholtz type and the Javal-Schiotz type. Both use the relationship between object size, image size and distance to calculate corneal curvature. The former is the more familiar to most ophthalmologists. It is a one-position device that uses adjustable image size and consists of aligning plus sign and minus sign mires. The latter is a two-position instrument that uses adjustable object size and requires alignment of a red square and green staircase design. Keratometers measure the size of an image reflected from two paracentral points on the cornea. The instrument contains doubling prisms to stabilize the image allowing more accurate focusing. The anterior corneal curvature is then obtained from the convex mirror formula and corneal power is calculated empirically using Snell's law of refraction with simplified optics. The keratometer measures the anterior corneal surface but uses an assumed index of refraction (1.3375 rather than the actual 1.376) to account for the small contribution from the posterior corneal surface, the corneal thickness, and also to allow 45 D to equal 7.5 mm radius of curvature (K (diopters) = 337.5/r). These simplifications and assumptions create a number of limitations. The keratometer only measures a small region of the cornea (i.e., 2 points at the 3-4 mm zone), and this measured region is different for corneas of different powers. No information is provided about the cornea central or peripheral to these points. Furthermore, the keratometer assumes that the cornea has a symmetric spherocylindrical shape with a major and minor axis separated by 90 degrees. It also does not account for spherical aberration, and it is susceptible to focusing and misalignment errors. Finally, distortion of the mires precludes accurate measurement of irregular corneas and cannot be quantified. [35]

1.3.2. CORNEAL TOPOGRAPHY AND TOMOGRAPHY

Corneal topography is used to characterize the shape of the cornea, similar to how one would characterize a mountain using a topographic map. Originally, corneal topography was only used to describe the anterior surface of the cornea. Devices now are able to characterize both the anterior and posterior corneal surfaces, creating a three-dimensional map (corneal tomography). Advances in digital photography and computer processing have vastly increased the utility of corneal topography. [36]

The first advancement in assessing the shape of the anterior corneal surface was made in the late 1800s with the development of the Placido disc. [36]

This technique characterizes the corneal surface by assessing the reflection of a set of concentric rings of the anterior corneal surface. As the image from the Placido disc is projected on the cornea, some of the light is reflected off the tear film-air interface like a mirror. The pattern of light reflection reveals the shape of the anterior surface of the cornea. [36]

A second technique for corneal topographic assessment is the scanning slit technique (*e.g.,* Orbscan). This method uses rapidly scanning projected slit beams of light and a camera to capture the reflected beams to create a map of the anterior and posterior corneal surface. A third technique, known as Scheimpflug imaging, uses a rotating camera to photograph corneal cross-sections illuminated by slit beams at different angles (*e.g.*, Pentacam). This method corrects for the non-planar shape of the cornea and, thus, allows greater accuracy and resolution in creating a 3-D map of the cornea. [37-39]

The Oculus Pentacam utilizes Scheimpflug technology to create topographic reports. The reports contain numerous informations, and samples of the overview report and the 4 maps report are provided below. Specifically, the overview report provides the Scheimpflug image, which is a cross-sectional image showing the cornea, anterior chamber, iris and lens. Three-D representation of the patient’s corneal shape is also provided. The density of the cornea is evaluated using densitometry, which is an objective measurement of light scatter in the cornea. Any densitometry value less than ~30 is considered normal; thus, a condition resulting in decreased corneal clarity (*e.g.*, corneal edema) will increase the densitometry value. There is also a convenient summary of the keratometry, pachymetry, and other numeric measurements in this report. A pachymetry color map indicates corneal thickness.

FIGURE 6. Pentacam image of cornea – with the rule astigmatism

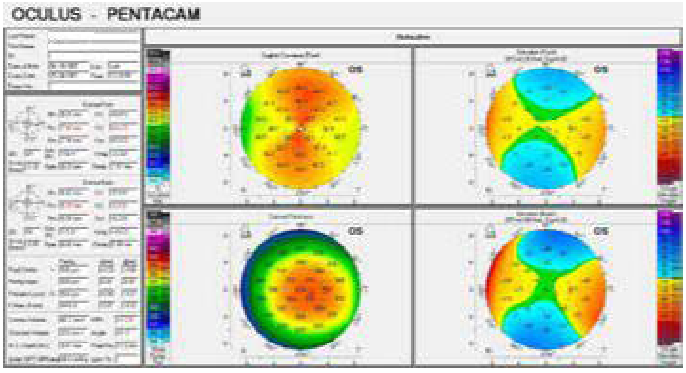


FIGURE 7. Pentacam image of cornea – oblique astigmatism

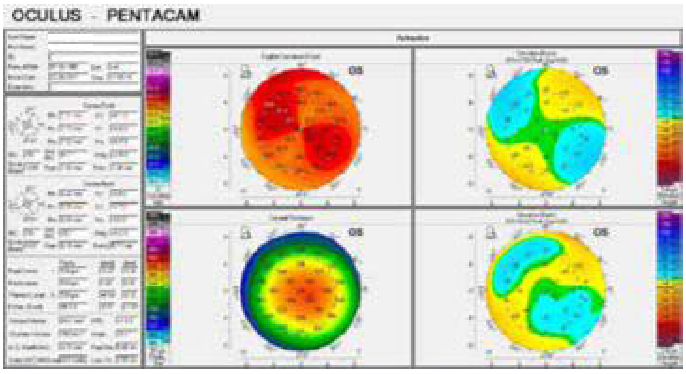


FIGURE 8. Pentacam image of cornea – against the rule astigmatism

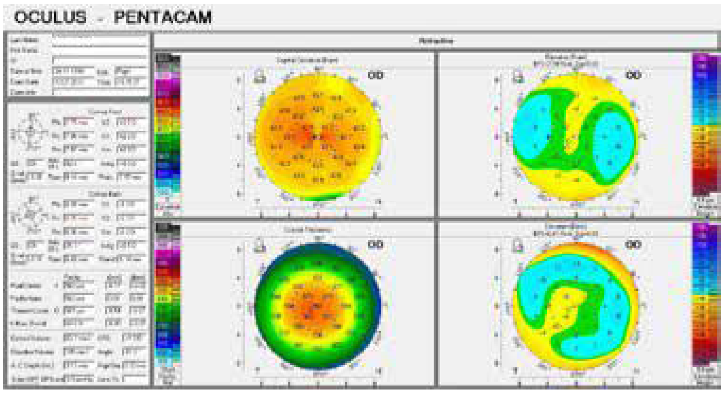
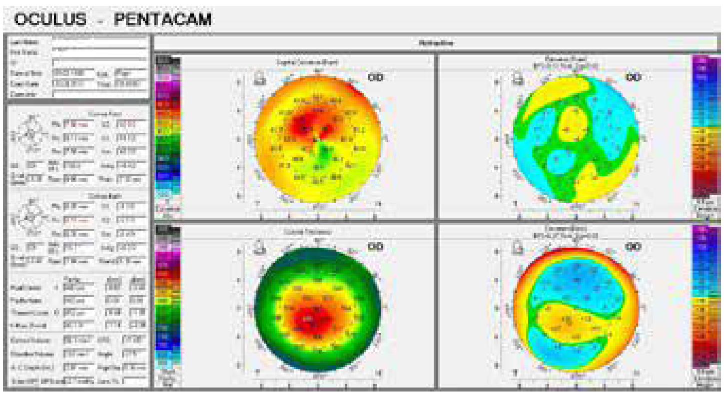


FIGURE 9. Pentacam image of cornea – irregular astigmatism



Pentacam report named “4 maps refractive” provides a summary of keratometry, pachymetry with map, and numeric measurements. Pentacam report includes the axial curvature map, also known as a sagittal map, depicts the curvature of the anterior corneal surface in dioptric values for each point. The color scale represents the power in diopters at each particular point. Warmer colors represent steeper corneal curvature while cooler colors represent flatter areas. Anterior float and posterior float images, which are elevation maps, are generated on the Pentacam report. Instead of displaying the refractive power of the cornea, elevation maps display the shape of the cornea by comparing it to a computer-generated best-fit sphere (*i.e.,* a perfect sphere that best approximates the corneal shape on average). Posterior float, similar to the anterior float, shows the shape of the posterior cornea compared to a best-fit sphere. For the elevation maps (anterior and posterior float), warmer colors denote where the cornea is elevated above the best fit sphere and cooler colors denote where the cornea is depressed below the best fit sphere. A pachymetry map is a color map that indicates corneal thickness; cooler colors are thicker and warmer colors are thinner. [40, 41, 42]

The main uses of corneal topography include pre-operative evaluation to rule out certain corneal abnormalities and postoperative evaluation to monitor the surgeon’s and laser’s performance. Moreover, corneal topographic analysis has become the standard of care in the pre-operative evaluation of all refractive surgical patients because of its ability to diagnose subclinical ectatic disorders. [40, 41, 42]

1.4. NON SURGICAL TREATMENT OF ASTIGMATISM

1.4.1. PRESCRIPTION SPECTACLES (EYEGLASSES)

Spectacles are the simplest way of correction. In general, lenses are made from three materials: plastic, glass, and polycarbonate.

The spectacle lenses for astigmatism correction have a toric or cylindrical surface in order to give a single focal point in the retina. It adjusts the direction of the incoming light rays, correcting the uneven curve of the cornea. The thickness of the lens is not the same across its surface. This difference in thickness is increased due to the strength of the astigmatism.

Spectacles are a choice of correction for people with regular astigmatism. They will contain a cylindrical lens prescription for the astigmatism in a specific meridian of the lens which designates the axis of the lens power. Higher degrees of astigmatism and more complex corrections (i.e. very high myopic or hyperopic astigmatism and mixed astigmatism) cannot accomplish optimal quality of vision with spectacle correction. In addition, irregular astigmatism cannot be corrected by a lens of the glasses. [43, 44]

1.4.2. CONTACT LENSES

1.4.2.1. SOFT CONTACT LENSES

Contact lenses sit right on the surface of the eye. Many different types of contact lenses are available on the market.

Soft contact lenses conform to the shape of the eye. They come in spherical and toric version. Their toric version can be used for astigmatism correction. They are readily available in several fitting designs. The astigmatic correction can be on the front or the back surface of the lens. Toric lenses typically have a mark to note the 6-o'clock position.

Contact lenses often provide better vision than do spectacles by masking irregular astigmatism (high orders of aberration). For mild to moderate irregularities, soft spherical, soft toric or custom soft toric lenses are used. Large irregularities typically require rigid gas permeable (RGP) contact lenses to mask abnormal surface; the anterior surface of the contact lens creates a new optic surface, and the tear film corrects the corneal irregularities.

1.4.2.2. RIGID GAS-PERMEABLE CONTACT LENSES

Rigid gas permeable contact lenses maintain their regular shape while on the cornea, and offer an effective way to compensate for the cornea's irregular shape and improve the vision of persons with astigmatism and other refractive errors. Parameters of RGP lenses are custom made for each patient. They come in spherical and toric version. Bi-toric designs are the most popular toric design in RGP contact lens practice, and represent the best choice if corneal toricity is less than or exceeds refractive astigmatism.

Some specialized RGP lenses have been developed specifically for keratoconus. Most provide a steep central posterior curve to vault over the cone and flatter peripheral curves to approximate the more normal peripheral curvature.

An alternative approach is to use hybrid contact lens that comprises a rigid center and a soft skirt. The hybrid lens theoretically provides the good vision of an RGP lens and the comfort of a soft lens.

Piggyback lens systems involve the fitting of a soft contact lens with an RGP lens fitted over it. This system may allow comfort benefits similar to those offered by hybrid lenses, as well as a greater choice of contact lens parameters.

Gas-Permeable Scleral Contact lenses have 2 primary indications: (1) correcting abnormal regular and irregular astigmatism in eyes that preclude the use of rigid corneal contact lenses, and (2) managing ocular surface diseases that benefit from the constant presence of a protective, lubricating layer of oxygenated artificial tears. [45, 46]

1.5. SURGICAL TREATMENT OF ASTIGMATISM

Surgical correction of astigmatism takes place chiefly in the corneal tissue, by the means of corneal incisional or corneal refractive surgery, or it is compensated with toric intraocular lenses. As mentioned before astigmatism also can be corneal or lenticular. Even if the astigmatism is lenticular in young population can be compensated with corneal refractive surgery.

1.5.1. INCISIONAL SURGERY

1.5.1.1. RADIAL KERATOTOMY

Radial keratotomy (RK) is now largely considered an obsolete procedure, but it did play an important role in the history of refractive surgery. [47]

Radial keratotomy (RK) as a refractive surgical procedure to correct myopia (nearsightedness) was finally completed and developed in 1974, by Svyatoslav Fyodorov, a Russian ophthalmologist.

In RK, incisions are made with a diamond knife. Incisions that penetrate only the superficial corneal stroma are less effective than those reaching deep into the cornea, and consequently, incisions are made quite deep. [48]

Radial corneal incisions severed collagen fibrils in the corneal stroma. This produced a wound gape with midperipheral bulging of the cornea, compensatory central corneal flattening, and decrased refractive power. The design of the diamond-blade knife (angle and sharpness of cutting edge, width of blade, and design of footplate) influenced both the depth and the contour of incisions. The footplates reduced the risk of penetration and stabilized the blade. The guard on the front of the blade prevented inadvertent entry into the central optical zone. The length of the knife blade and the associated depth of the incisions were set according to the corneal thickness, which was usually measured with an ultrasonic pachymeter. The ideal depth of RK incisions was 85-90% of the corneal thickness. [49]

Potential serious complications include loss of best-corrected visual acuity, perforation of the cornea, infection and rupture of the globe. Some of the major concerns with this procedure relate to the significant corneal instability induced by the surgery, including diurnal fluctuation of refractive error, overcorrection, hyperopic shift and potential rupture of the globe with blunt trauma. [50]

Although ophthalmologists do not initially perceive radial keratotomy as a means for correcting astigmatism, it follows that if it selectively flattens the cornea more in some meridians, the ophthalmologist are effectively correcting astigmatism. Although the predictability is slightly less in correcting astigmatism than that for correction of myopia, there is an opinion that it is still rather good option for astigmatism treatment. [51]

1.5.1.2. ASTIGMATIC KERATOTOMY AND LIMBAL RELAXING INCISIONS

Astigmatic keratotomy, surgical procedure, was first performed in 1885 by Schiötz, a Norwegian ophthalmologist. [52]

Several techniques of incisional surgery have been used to correct astigmatism, including transverse (straight) and arcuate (curved) keratotomy (AK), in which incisions are typically placed in the cornea at the 7 mm optical zone; and limbal relaxing incisions (LRIs), which are placed at the limbus.

Arcuate keratotomy is an incisional surgical procedure in which arcuate incisions of approximately 95% depth are made in the steep meridians of the midperipheral cornea at the 7 mm optical zone and have greater relative depth. LRIs are incisions set approximately 50 microns less than the thinnest pachymetry measurement at the limbus, and placed just anterior to the limbus. Due to concomitant steepening of the orthogonal meridian AK and LRI correct astigmatism without inducing substantial hyperopic shift of the spherical equivalent of the preoperative refraction. LRIs achieve increased effect primarily by increasing the length of the incision. For AK, cylindrical correction can be increased by increasing the length or depth of the incision, using multiple incisions, or reducing the optical zone. The longer and deeper the incision and smaller the optical zone, the greater the astigmatic correction. [53, 54]

The outcome of AK and LRI surgery depends on several variables, including patient age; the distance separating the incision pairs; and the length, depth, and number of incisions. Few large prospective trials have been performed. The Astigmatism Reduction Clinical Trial (ARC-T) of AK, which used 7 mm optical zone and varying arc lengths, showed a reduction of astigmatism of 1.6 ± 1.1 D in patients with preoperative, naturally occuring astigmatism of 2.8 ± 1.2 D. Other AK studies have shown a final uncorrected distance visual acuity (UDVA) of 20/40 in 65-80% of eyes. Overcorrections have been reported in 4-20% of patients.

Studies of LRIs are limited, but these incisions are frequently used with good results in astigmatic patients undergoing cataract surgery. [55]

With development of new surgical techniques for treatment of refractive errors, we can conclude that both, astigmatic keratotomy and radial keratotomy did not show effective results because scars on cornea never heal complitely, treated corneas are prone to infections and there is a tendency to hyperopic shift – they are not completely predictable.

1.5.2. INTRACORNEAL RING SEGMENTS

Intrastromal corneal rings (ICR) are designed for modification of the corneal curvature. Intrastromal rings act as spacers inside the corneal stroma, leading to decreasement of central part of the cornea with the maintenance of physiological corneal curvature. They are usually implanted in the cornea at posterior 70 to 80% stromal depth through channels made mechanicaly or with the femtosecond (FS) laser. [56, 57] Titration of refractive correction is achieved with change in implantation thickness. [58] They are made of polymethilmetacrilate (PMMA), and are implanted deep in stroma on middle periphery of cornea leaving the pupillary area intact. Primarly were developed for treating nearsightness, but nowadays are used for treating keratoconus. [59, 60]

Four types of intracorneal rings are available on the market, and they vary in diameter and geometrical profile (INTACS, Ferrara rings, Bisantis segments, Myoring). This method is reversible, and leads to satisfying decreasement of spherical equivalent and better remodeling of keratoconic corneas, but it does not stop the progression of the disease, so nowadays is used in combination with the crosslinking technique. [60-63]

Cases of too shallow insertion of intrastromal corneal rings, endothelial perforations, postoperative migration of rings, stromal necrosis of cornea and infectious keratitis are reported as complications. [64, 65]

1.5.3. EXCIMER LASER SURGERY

1.5.3.1. SURFACE ABLATION

Photorefractive keratotomy (PRK)

Photorefractive keratotomy was developed on the idea of change in corneal curvature by means of ablating corneal tissue. The direct reshaping of the cornea's central optical zone using tissue ablation was achieved with far ultraviolet radiation. This type of surgery was first theorized by New York ophthalmologist, Doctor Steven Trokel. Stephen Trokel in collaboration with Srinivasan Rangaswamy performed the first photorefractive keratectomy surgery in Germany. [66, 67]

The first PRK procedure in a sighted eye was performed in 1987 by Theo Seiler, then at the Free University Medical Center in Berlin, Germany. [68]

The PRK method involves mechanical removal of the epithelium (the renewable superficial layer of the cornea) and then remodeling of the cornea with an excimer laser. The epithelium used to be removed with a knife or a rotating brush. Today the epithelium is generally removed mechanically in cases of repeated surgery and in case of certain irregularities of the cornea, while in other cases it is usually removed with laser and then it is called Trans-PRK (T-PRK). After the treatment a "wound" is left on the eye which needs 3-5 days to heal. The surgery itself is not painful, but the postoperative recovery in case of this method can be uncomfortable. Generally, the recovery of visual acuity depends on the epithelial healing. Complete stabilization of vision quality often takes up to several weeks. The operation is generally suitable for patients with negative diopter values, up to -10.0 D with astigmatism up to -3.0 D, in mild irregularities of the cornea, in cases of a thin cornea and corneal scars. Hyperopic patients and patients with astigmatism with more than -/+ 3.0 D are not most suitable candidates for PRK method because of the high degree of diopter regression. [69, 70]

When treating astigmatism with PRK method there is also a problem with residual astigmatism. It may occur based on the individual's surface healing; some patients may end up with a small amount of irregular astigmatism secondary to the adjustment of epithelial cells and keratocytes. [71]

The main advantage of PRK over Laser in situ keratomileusis (LASIK) is an absence of creation of the corneal flap and thus flap related complications. In addition, since there is no flap (which contains both epithelial and the deeper stromal tissues and does not contribute to corneal biomechanical stability) less tissue is removed with spherical or spherocylindrical correction leaving the cornea more biomechanically stable. It is also speculated, since there is no transection of deep corneal nerves, that PRK may have decreased incidence of postoperative dry eye. [67]

In general, problems with PRK include time measured in days for epithelium to recover, followed by consequent pain while recovering and incidence of corneal haze. Corneal haze development is thought to be secondary to side effects of the cornea's innate wound healing mechanisms.

Animal studies showed that, following PRK, there is an initial apoptosis of keratocytes. In response, some keratocytes undergo transformation to myofibroblasts. Additionally, the extracellular matrix produced by myofibroblasts is disorganized and denser than the usual matrix, and consequently scatters more light causing a haze. Incidence of haze has declined since refractive surgeons started using the medicine mitomycin C directly following the laser procedure. [72]

The use of topical corticosteroids to modulate postoperative wound healing, reduce anterior stromal haze, and decrease regression of the refractive effect refractive effect remains controversial.

Regarding all the above there was obviously a need for development of some new method to get around the problems by keeping the epithelium and Bowman's membrane as uninterrupted as possible. PRK served patients well in the past, and still does for a select few. PRK is still the preferred option for those with thin corneas, corneal dystrophies, corneal scars, or recurrent corneal erosion. [73, 74, 75]

1.5.3.2. LASER IN SITU KERATOMILEUSIS (LASIK)

In 1990, two ophthalmologists enhanced PRK method by developing what would later become LASIK. The term keratomileusis comes from the Greek words for “cornea” (kerato) and “to carve” (mileusis). Laser in situ keratomileusis, which combines keratomileusis with excimer laser stromal ablation, is currently the most frequently performed keratorefractive procedure because of its safety, efficacy, quick visual recovery and minimal patient discomfort. LASIK combines two refractive technologies: excimer laser stromal ablation and creation of a corneal flap.

Greek ophthalmologist Ioannis Pallikaris and Italian ophthalmologist Lucio Burrato developed two types of what was then known as “flap and zap”. Instead of working on top of the corneal surface, these doctors used a blade to cut a thin flap in the cornea, zap the tissue underneath, and replace the flap like a natural bandage. The flap allowed for less discomfort and a faster recovery. [76]

In 1991 Pallikaris et al. reported usage of a modified microkeratome (an automated electric knife) for creation of nasally based central corneal flaps which were allowed to heal with a bandage soft contact lens, using neither sutures nor bioadhesives. The optical quality of the corneas was excellent with maintained transparency and lack of distortion of the corneal surface which led to conclusion that the concept of the flap technique may be useful in laser in situ keratomileusis. [77]

In 1993 Lucio Burrato reported one year follow up after myopic keratomileusis with the excimer laser and found that excimer laser myopic keratomileusis is an effective way to correct high myopia and may be more accurate than other methods of keratomileusis. A plano corneal disc was cut with a Barraquer-Krumeich-Swinger (BKS) 1000 microkeratome, followed by argon fluoride excimer laser ablation of the stroma. [78]

Nowadays, LASIK is a lamellar laser refractive procedure which includes two steps. The first step is creation of the flap (partial-thickness lamellar corneal flap) usually created with the help of microkeratome or femtosecond laser. This method has become a popular method of refractive surgery, as it provides effective results and a short healing time. Indications for surgery are diopter values from -10.0 to +6.0, and up to ± 6.0 cylinders of astigmatism. [79-82]

The flap, which averages in thickness from 90 to 130 micrometers (μm), is folded back to expose the underlying stroma. The excimer laser system is then focused and centered over the pupil and the patient is asked to look at the fixation light. After the ablation is complete, the flap is replaced onto the stromal bed. The physiological dehydration of the stroma by the endothelial pump will begin to secure the flap in position in several minutes. Patients are instructed not to rub or squeeze their eyes. [83-88]

The main advantage of LASIK over PRK is related to maintaining the central corneal epithelium. This increases comfort during the early post-operative period, allows for rapid visual recovery, less discomfort after surgery and reduces the wound healing response. Reduced wound healing correlates with less regression for high corrections and a lower rate of complications such as significant stromal opacity (haze). Many advantages are related to preservation of the central corneal epithelium and epithelial basement membrane during LASIK. [87]

However, LASIK is not without complications. The creation of the lamellar flap during the LASIK procedure increases the risk of intraoperative and postoperative complications. Flap related complications such as incomplete or perforated flaps, intraoperative or postoperative flap distortions account for up to 15% of complications. Those complications are much higher with mechanical microkeratomes than femtosecond laser. From postoperative complication there are deep lamellar keratitis as non-infectious complications, and extremely rare microbial inflammations. The potentially most devastating late postoperative complication is corneal ectasia which is directly linked to severed corneal biomechanics caused by abundant thinning of the cornea. Other complications are prolonged dry eye, reduced vision in low lighting conditions, and visual distortions such as glare and haloes can still occur in up to 1-2% of cases. [86, 89]

1.5.4. LENS SURGERY

1.5.4.1. PHAKIC LENSES

For patients not suitable for corneal surgery, implantation of phakic intraocular lens (pIOL) can be a good alternative. [90]

Phakic lenses PIOLs have the advantage of treating a much larger range of refractive errors than can be treated safely and effectively with corneal refractive surgery. Phakic IOLs have a number of advantages such as preserving corneal tissue and decreasing the risk of ectasia, maintaining the corneal shape without inducing high order aberrations and the possibility of pIOL removal. [91]

PIOLs are removable, therefore, the refractive effect should theoretically be reversible. Implantation of these lenses has the advantage of preserving natural accommodation and compared with refractive lens exchange has lower risk of endophthalmitis and postoperative retinal detachment because of the crystalline lens barrier which is preserved and there is a minimal vitreous destabilization.

Currently, there are two types of pIOL: anterior chamber pIOL and posterior chamber pIOL.

1.5.4.1.1. Anterior chamber phakic IOLs

Anterior chamber pIOLs can be divided as (1) iris-fixated IOLs and (2) angle-supported IOLs.

Angle supported lenses are not in use any more, while iris fixated lenses come in rigid and foldable version. The diopter range of those lenses is from -3.00 D to -23.50 D, and from +1.00 D to +12.00 D in 0.50 D steps. Toric version is also available in minus cylinder notation to up to 7.50 D. [92-97]

Iris-fixated toric phakic IOLs are available in both rigid PMMA (Verysise toric, Artisan toric) and foldable silicone (Artiflex toric) versions. The rigid lens has 5.0 mm optic, while the foldable version has 6.0 mm optic. Both lenses have a total diameter of 8.5 mm and are available in spherical ranging from -3.00 D to -23.50 D and +2.00 D to +12.00 D, with cylinder powers ranging from 1.00 D to 7.00 D in 0.50 D steps. [98, 99]

1.5.4.1.2. Posterior chamber phakic IOLs

Posterior chamber pIOLs are placed behind the pupil and in front of the lens with haptics placed in sulcus. At this moment posterior chamber pIOLs are the prefered (most commonly implanted). The diopter range of those lenses is from -1.00 D to -18.00 D, and from +1.00 D to +8.00 D in 0.50 D steps. Toric version is also available in minus cylinder notation to up to 6.00 D. [100]

1.5.4.2. REFRACTIVE LENS EXCHANGE-CLEAR LENS EXTRACTION

Refractive errors can also be resolved surgically by IOL implantation procedure, called refractive lens exchange. For astigmatism correction toric IOLs are used. Those lenses have different powers in different meridians of the lens. They also have alignment markings on the peripheral part of the lens that enable the surgeon to adjust the orientation of the IOL inside the eye for optimal astigmatism correction. Achieving success with toric IOLs depends on the selection of suitable patients. Depending on the toric IOL model, the minimal available toric IOL power at the IOL plane is 1.00 D or the 1.50 D. At the corneal plane, this corresponds to a minimal corneal power of approximately 0.75 to 1.00 D, respectively. Taking into consideration the amount of astigmatism induced by the surgery, patients must have a corneal astigmatism of at least 1.00 to 1.25 D in order to be candidates for a toric IOL. Regarding corneal astigmatism patients with regular bow-tie astigmatism are most suitable for toric IOL implantation. Corneal topography is therefore important for detecting irregular astigmatism and keratoconus. [101, 102]

Astigmatism correction with Toric IOL does not affect the cornea. [103]

There are two types of toric version of IOLs – toric monofocal lenses and toric multifocal lenses.

Toric monofocal lenses have one spherical component combined with astigmatism component. They are designed to correct for distance vision, while near vision is corrected with spectacles.

Toric multifocal lenses can have bifocal, trifocal or extended depth of focus optics designed to correct vision at all distances. [103]

1.6. ASTIGMATIC LASER IN SITU KERATOMILEUSIS

When treating astigmatism several factors must be carefully considered:

- Residual error can be present despite all efforts
- The residual axis may be disturbingly different from the preoperative axis

Regular astigmatism is mainly generated by excessive corneal toricity. Corneal toricity can be suppressed either by flattening the steepest meridian to match the curvature of the initially flatter meridian or by steepening the flattest meridian to match the curvature of the initially steeper meridian. Simple myopic and hyperopic astigmatic treatments rely on the use of negative and positive cylinder modes, respectively. Compound and mixed astigmatism are treated by the combination of negative and/or positive cylindrical and spherical modes. When dealing with high compound astigmatism deeper ablation is required and thus, a greater curvature gradient between the center and periphery is created. [104]

Standard ablation patterns for astigmatic correction treat only the steeper meridian, leaving the flatter meridian unchanged. This, in turn, creates poor transition zones along the steeper meridian and unphysiologically abrupt dioptric curvature gradients, resulting in a midperipheral multifocality of the cornea. The poor transition zones achieved by treating only one meridian lead to an abnormal healing response, and cause an overcorrection of the sphere and under-correction as well as regression of the cylinder. [105]

Mixed astigmatism remains one of the most challenging defects for refractive surgery. Advancements in the correction of mixed astigmatism include pursuit of a postoperative corneal surface that is as symmetrical as possible, centrally as well as in the periphery. [106]

In the past several ablation patterns have been proposed for the treatment of mixed astig-matism: correction on the steep meridian (myopic cylinder ablation + hyperopic sphere ablation), correction on the flat meridian (hyperopic cylinder ablation + myopic sphere ablation), cross-cylinder ablation, and bitoric ablation (asymmetrically split on two meridians). [107-109]

Azar, in a thorough analysis of various available methods, recommended correction on the hyperopic meridian only with the advantage of removing less cornea than with any other technique. [110]

1.6.1. CORNEAL BIOMECHANICAL RESPONSE

A revolutionary approach to the problem of unpredictability has been introduced by Cynthia Roberts with the concept of corneal biomechanical response to laser ablation.[111]

The concept is based on the anatomical lamellar structure of the corneal stroma and on its tensile strength: central severing of lamellae due to creation of new refractive surface by excimer laser tissue removal causes elastic contraction of the remaining peripheral lamellae with consequent corneal curvature variation. This results in peripheral corneal increase in curvature, thickness and central flattening, leading to refractive change just where the curvature was carefully modified to achieve a planned power.

A delicate point in the creation of a new surface with excimer laser ablation is transition zone. In both stromal and surface ablation, marked variation of curvature in this peripheral portion leads to a response aimed to reduce curvature variation, but may induce regression and restriction of the effective optical zone. [111]

1.6.2. CYCLOTORSION

Cyclotorsion is the rotation of an eye around its visual axis. Throughout the LASIK procedure, cyclotorsion of the globe occurs continually, leading to misalignment of the axis if this effect is not taken into consideration. Cyclotorsion can lead to a decrease in the amount of astigmatism reduction. Mean cyclotorsion of the human eye during laser application in the supine position [112, 113] has been calculated to be 2.670 ±1.588°. With 10° deviation of an astigmatic ablation from the intended axis, approximately one-third of the astigmatism-correcting effect is lost, and with 20° of axis deviation, approximately two-thirds of the effect is lost. Misalignment greater than 30° produces a net worsening of astigmatism. [112, 113]

Bharti et al. [114] found that active cyclotorsion compensation during LASIK for myopic astigmatism increases the accuracy of cylinder correction.

Extensive cyclotorsional movement is a clinical reality, and it can result in significant optical errors. Since laser ablation applies unaccounted eccentric focal ablations, cyclotorsion during ablation may cause inaccurate positioning of spots, hypocorrection, cylinder axis deviation, and induction of aberrations. Postoperative high order aberrations may be less tolerated than residual refractive error, and cannot be corrected with spectacles. Compensation with automated cyclotorsional tracking is necessary to optimize the benefits of ablations. [115]

1.7. MICROKERATOME

First manual mechanical microkeratome was designed by José Ignacio Barraquer in 1958, and was intended for keratophakia and frozen keratomileusis. [116]

First mechanical (automated) microkeratome with nasal hinge – Castrovievo microkeratome was built in 1963. Automated microkeratomes came into clinical use in 1991 for automated lamellar keratoplasty with Ruiz and Lenchig's Chiron and were called "automated corneal shaper". [117]

Modern microkeratomes available on today's market can create all sorts of adjusted flaps. Every microkeratome has its specific characteristics that determine size, shape and thickness of the flap together with size, shape and position of the hinge. Today's microkeratomes offer high level of security, but the risk of complications is still not completely eliminated. [83]

Microkeratome is an automated electric knife, which works like a carpenter's plane and is used for the creation of the corneal flap. Before the surgery, the microkeratome and vacuum unit are assembled, inspected and tested to ensure proper functioning. After a suction ring has been properly positioned, suction is activated. The suction ring has 2 functions: to adhere to the globe, providing a stable platform for the microkeratome cutting head; and to raise the IOP to a high level, which stabilizes the cornea. Intraocular pressure should be raised to over 65 mmHg. The dimensions of the suction ring determine the diameter of the flap and the size of the stabilizing hinge. The thicker the vertical dimension of the suction ring and the smaller the diameter of the ring opening, the less the cornea will protrude, and hence a smaller-diameter flap will be produced. The suction ring is connected to a vacuum pump, which is typically controlled by an on–off foot pedal. Hinge positions, nasal or superior, depend on the design of the microkeratome, and are at the surgeon's discretion. [83, 117]

First generations of microkeratomes had problems during LASIK surgery, such as loss of suction, creation of flaps with irregular edges and wide variations of thickness and shape of the flaps. In the last three decades the quality, speed, precision and efficacy of mechanical microkeratomes have been constantly improving, which led to a significant increase in safety and precision of the surgery.

Last generations of microkeratomes allow very precise flap creation with regular edges and predetermined thickness and shape. The procedure lasts only few seconds and does not create any discomfort to the patient. Flaps are usually 90-100 μm thick which makes a huge improvement compared to flaps created with older types of microkeratomes.

Microkeratomes are devided according to the movement of dissection head. Nowadays mostly used microkeratomes use linear, arcuate or pendular movement.

Linear movement (translation) – dissecting head is lead over two parallel tracks in horizontal plane. Linear microkeratomes have an option to create only nazal hinge. (Table 1)

Arcuate movement (translation) – dissecting head is lead over horizontal plane over eccentric axis circular track. Arcuate microkeratome has multiple options for hinge position. (Table 1)

Pendular movement (translation) – dissecting head is lead like a swing over a horizontal plane above corneal apex. Part of a vacuum ring, in touch with cornea, has a convex shape, and dissecting head is in a shape of hemisphere which ensures constant thickness of the flap. (Table 1)

Microkeratomes for single and multiusable purposes

Majority of microkeratomes are reusable after disassembling, cleaning and sterilization. Only exception is the blade which is always exclusively made for single use. All peripheral components – silicone tubes, dissecting head with previously inserted blade, and vacuum rings can be created only for single use.

TABLE 1. Display of basic characteristics of comercially available microkeratomes

MANUFACTURER	MODEL OF MICROKERATOME	TYPE OF MOVEMENT	FLAP THICKNESS	STANDARD DEVIATION (μm)	FLAP SIZE (mm)	HINGE POSITION
ZIEMER	Amadeus II[168,169]	Linear	140-160-200-250-300-350-400-450	Not available	8,5-10	Superior/nasal
MORIA	M2 single use 90[168, 170] SBK One Use + 90[168, 171]	Arcuate Linear	110-130 100	±15 ±8	8-11 8,8-10,5	Superior Nasal
MED Logics	ML 7[168, 172]	Linear	100-130	±9	7,5-10	360° – possibility of choosing the Position
SCHWIND	Carriazo-Pendular[168, 173]	Pendular	90-110-130-150-170	±10-12	9-10	360° – possibility of choosing the Position
Data about characteristics and performance of microkeratomes available at manufacturers links [83, 180-184]						

1.8. FEMTOSECOND LASERS

Femtosecond laser technology was first developed by Dr. Kurtz at the University of Michigan in the early 1990s[118] and was rapidly adopted in the surgical field of ophthalmology.

1.8.1. PHYSICAL PRINCIPLES OF FEMTOSECOND LASERS

Femtosecond lasers emit light pulses of short duration (10^{-15} s) at 1053 nanometers (nm) wavelength that cause photodisruption of the tissue with minimum collateral damage. [119-122] This enables bladeless incisions to be performed within the tissue at various patterns and depth with high precision.

Femtosecond lasers are solid state lasers and can be focused anywhere within the cornea where the energy can be raised to a threshold such that a plasma is generated. [123]

Laser is based on the principle of nonlinear apsoption (which means that corneal tissue is transparent for infrared laser radiation of moderate intensity and it doesn’t lead to apsorption) and on the principle of photoionisation (laser induces optical break down), which leads to photodisruption in a focal point. The final result is creation of fast spreading cloud of free ions and ionisating molecules (plasma). Small volumes of tissue are vaporised with formation of cavitation bubbles of gas that gradually spread in nearby tissue, and they consist of carbon dioxide and water. Main characteristics of femtosecond laser is that it is possible that low energy of pulse can achieve high power. [124-131]

The femtosecond laser is used primarily to create a LASIK flap within the corneal stroma. The laser allows precise control of flap architecture not obtainable with a traditional mechanical microkeratome. [132-134] Once the LASIK flap is created, an excimer laser is used to reshape the cornea.

Nowadays creation of the flaps in LASIK procedure with the use of femtosecond lasers is becoming more and more popular, because of its advanced precision of creation controlled by laser beams and higher intraoperative safety (lower risk of intraoperative complications), and the future of refractive surgery is heading to that direction. [135, 136] Femtosecond lasers have growing popularity in ophthalmic surgery and besides flap creation, which is their most common use, they are also used for relaxing limbal incisions, astigmatic keratotomies, creation of intrastromal tunnels for intracorneal ring segments and intrastromal pockets for inlay insertion and also drug delivery. Nowadays, they are also used as a single refractive devices in refractive surgery with a novel refractive surgery procedures such as Refractive Lenticule Extraction (ReLex Flex), Small incision lenticule extraction (ReLex Smile) and presbyopia correction in terms of Intrastromal presbyopia correction (Intracor) procedure. Different types of femtosecond lasers are also introduced in cataract surgery and are able to perform incisions, capsulorhexis and lens fragmentation.

1.9. EXCIMER LASERS

1.9.1. EXCIMER LASER PRINCIPLE OF WORK

The excimer laser is based on the combination of two gases: a noble gas and halogen. Both of these are generally stable in their normal low-energy state. When a high-voltage electrical discharge is delivered into the laser cavity containing these gases, the gases combine to form a higher energy excited-gas state compound. The term “excimer” is derived from a contraction of “excited dimer”. On the dissociation of this high-energy compound, a photon of energy is released that corresponds to the bond energy of the noble gas-halogen molecule. [137, 138]

This wavelength of light energy is amplified in the laser system, resulting in the production of a discrete high energy pulse of laser energy. The specific wavelength of an excimer laser depends on the composition of the gases used in the laser system. Excimer laser systems in current clinical use rely on argon and fluorine gases. The argon-fluorine excimer lasers emit energy at a wavelength of 193 nm. This wavelength falls in the UV-C range of the light spectrum. In contrast, the krypton-fluoride excimer laser used in early laboratory studies emits a wavelength of 248 nm. [139, 140]

Laser energy at 193 nm is very well absorbed by the proteins, glycosaminoglycans and nucleic acids comprising the cornea. Since 193 nm photon is of higher energy than the molecular bond strength of these compounds, absorption of the laser energy results in breaking of the bounds. The resulting molecular fragments are ejected from the surface of the cornea at supersonic speeds. [140-142]

It is important to understand that the excimer laser does not cut tissue like a scalpel; rather it ablates or removes tissue from the corneal surface. The ablated material appears as an effluent plume that upon analysis has been shown to consist of a variety of high-molecular-weight hydrocarbons. [143]

There is a concern about the potential for mutagenesis or carcinogenesis with any laser radiation, especially in the ultraviolet light spectrum. Studies have been done showing that the 193 nm excimer laser is neither mutagenic nor carcinogenic. [144, 145]

This may be in part a result of shielding of the nucleus by the cell’s cytoplasm.

Several attributes of the argon-fluoride excimer laser ablation make it particularly appropriate for corneal sculpting. The laser energy is well absorbed near the corneal surface and, thus, should have few deep direct or secondary mechanical (shock-wave) effects on the corneal tissue. The ablation process is rapid, and excess energy is ejected with the effluent plume. [145]

There is minimal thermal damage to the surrounding tissue. Because of these qualities, the 193 nm excimer laser can be used to meticulously reshape large areas of the corneal surface while minimizing damage to remaining tissue. [146]

The excimer laser technique is qualitatively different from refractive surgical techniques such as radial or astigmatic keratotomy, which achieves corneal reshaping through biomechanical changes mediated through thin knife incisions.

1.9.2. TYPES OF EXCIMER LASERS

The first-generation excimer lasers were “broad beam lasers” or “full beam lasers“ that created less uniform surface profiles than the newer generations. Full beam enables faster treatment (for given frequency) and is less sensitive for decentration, but homogenizes slower, gives irregular treatment of the surface and has more expressed thermal effect. It is needed to use masks for achievement of desired treatment form, and it is not possible to perform custom treatments. [146]

Newer-generation of excimer lasers use scanning beams or flying spots, with smaller spot sizes and more efficient eye trackers. Systems for scanning slit delivery act like flying spot systems and it exceled some limitations of full beam systems, but maintained the speed of the treatment and low decentration sensitivity. System uses additional diaphragm between full beam and the eye, which flows through hexagonal beam of a smaller diameter (10 mm x 1 mm) to the eye, and improves homogeneity of the beam. Ablation masks rotate, enabling performance in different directions. [146]

Flying spot systems convert laser beam in small round spot (between 0.6 and 2.0 mm). System uses only central most homogenic part of the beam, and beam direction is controlled by a mirror with rotation function. Ablation of targeted tissue is performed by repeated delivery of high number of pulses, in which every pulse removes only small area of tissue. Very high frequency is needed to shorten the treatment period, especially if the spots are very small. Also, spots need to be distributed precisely to avoid thermal effect. During that time eye tracking system is obligatory, because it is very sensitive to decentration. Energy profile of every spot is Gaussian and enables smooth areas of ablation, and the distance between two aiming spots is half of a beam size so the regular ablation can be provided. Main advantage of these systems is possibility of treatments high levels of irregularities. The smaller the spot, the treatment option of irregularities is higher. [146]

Although excimer machines from different manufacturers converge in technology, individual lasers differ in laser ablation algorithm, eye-tracking technology, frequency of laser ablation, corneal thickness ablated, duration of treatment, and physical design.

1.9.2.1. Pulse duration

Pulse arises during highest instability of excited dimer (half-time break up from 9 to 23 ns) and lasts 10 to 20 ns. The shorter the pulses, the less influence of thermal effect is on the nearby tissues. [146]

1.9.2.2. Pulse frequency

Frequency of pulses (number of pulses emitted in a second) varies from 10 to 1050 Hz depending on laser model. The higher the frequency – treatment is faster, but the thermal effect is higher, so the cooling of the treated tissue is ensured by using different algorithms. Optimal laser frequency with full beam is from 10 to 50 Hz, while with flying beam lasers it goes up to 1050 Hz, and the speed depends on success of algorithm for positioning sequent pulse strikes. [146]

1.9.2.3. Pulse energy

Energy that the pulse is delivering varies from 10 to 250 mJ depending on the laser. Difference in pulse energy can be up to 10%. During typical refractive procedure variation on the depth of tissue penetration is ±0,1% (which corresponds to 0,1 D) so it is negligible in clinical practice. [146]

1.9.2.4. Constant energy of radiation on measured area

Step of photoablation on the corneal surface of 193 nm wavelenght is 50 mJ/cm^2. Below this step photoablation is irregular and incomplete. Every pulse with constant energy of radiation above minimal step precisely removes certain amount of corneal tissue. Amount of tissue that pulse removes is increasing linearly with energy increase up to the values of 600 mJ/cm^2. After that value, increase of radiation energy is not increasing the amount of tissue removed by pulse. Constant radiation energy depends on the type of laser, and goes from 160 i 250 mJ/cm^2. [146]

1.9.2.5. Degree of ablation

Degree of ablation goes from 0,25 to 0,6 μm by pulse hit, and is typical for every laser. Many factors have influence on ablation degree. Every histological layer of the cornea has different ablation degree (ablation of epithelium is faster than stromal ablation, while stromal ablation is 30% faster of Bowman's membrane ablation). Scaring slows down the ablation, while dehydration of the tissue accelerates it. [146]

Conventional laser refractive surgery platforms are capable of correcting lower-order aberrations, such as hyperopia, myopia, and astigmatism. Higher-order aberrations (HOAs) such as coma, spherical aberration and trefoil are induced by, and remain uncorrected in traditional laser in situ keratomileusis (LASIK) surgery. [147, 148]

The HOAs call for more advanced optical measurements and more sophisticated laser algorithms. These laser algorithms are found in wavefront (WF) based treatments, which have been shown to diminish induced HOAs compared to traditional LASIK, and increase predictability of visual outcomes. [147-157]

1.9.3. COMMERCIALY AVAILABLE EXCIMER LASERS

Wavelight Allegretto – is a flying-spot excimer laser, with a pulse repetition rate from 200 to 500 Hz depending on the laser model, with two galvanometric scanners for positioning laser pulses. The beam is a small-spot, <0.95 mm in diameter, with a Gaussian energy distribution. It has a short treatment time of 2 seconds per diopter. The system has an infrared high-speed camera operating at 400 Hz to track the patient's eye movements that either compensates for changes in eye position or interrupts the treatment if the eye moves outside a present predetermined range. The tracker has automatic pupil cantering and an integrated cross-line projector for alignment of the head and eye position, with a "NeuroTracker" for cyclotorsion control for the wavefront-optimized algorithm. Its eye-tracker system and laser trigger are synchronized. Its optimized ablation profile is designed to maintain a more natural corneal shape by adjusting for the asphericity of the cornea based on the anterior curvature readings (providing more treatment to the periphery than centrally), and minimizing the amount of spherical aberration induced during surgery. [158, 159] The laser also features the ability to perform custom treatments (topography guided). The company supplies a nomogram chart, which recommends a standardized reduction in treatment for high degrees of myopia and cylinder. For low myopia, an increase in treatment is recommended instead. (Table 2)

FIGURE 10. Wavelight Allegretto Eye-Q 400 Hz laser platform

Schwind Amaris – is a flying-spot excimer laser with a pulse repetition rate of 500 to 1050 Hz depending on the laser model and produces a beam size of 0.54 mm Full-Widthat-Half-Maximum (FWHM) with a super Gaussian ablative spot profile. It has a short treatment time of less than 2 seconds per diopter. Inside the software package the laser is able to perform aspheric and custom (topography and ocular guided) treatments. Its aspheric ("Aberration-FreeTM") ablation algorithm is designed to maintain the preoperative levels of ocular higher-order aberrations. [160-163]

Aspheric aberration neutral [164] (Aberration-FreeTM [165] profiles are not based on the Munnerlyn proposed profiles, [166] and go beyond that by adding some aspheric characteristics to balance the induction of spherical aberration (prolateness optimization). The profile is aspherical-based, including a multidynamic aspherical transition zone, aberration and focus shift compensation due to tissue removal, pseudo-matrix based spot positioning, enhanced compensation for the loss of efficiency, and intelligent thermal effect control; all based on theoretical equations validated with ablation models and clinical evaluations.

Depending on the planned refractive correction, approximately 80% of the corneal ablation is performed with a high fluence level (>400 mJ/cm²) and this leads to a considerable reduction in time spent treating the cornea. Fine correction is performed for the remaining 20% of the treatment using a low fluence level (<200 mJ/cm²), aimed to reduce the amount ablated per pulse and smooth out the ablated stromal bed. The laser features a six-dimensional 1050 Hz infrared eye tracker with simultaneous limbus, pupil, iris recognition, and cyclotorsion tracking integrated in the laser delivery process. (Table 2)

FIGURE 11. Schwind Amaris 750S laser platform

Mel (Carl Zeiss Meditec AG, Jena, Germany) – available in two laser models (Mel 80 and Mel 90–250 Hz, 500 Hz). Laser has Gaussian profile of laser beam with aiming spot of 0,7 mm. Overheating of corneal surface is controlled with nonrandomised arrangement of aiming spots, and atmosphere and homogenisation of ejected gasses over cornea is controlled with specially designed extension. On 500 Hz model eye tracker system works in infrared spectrum on a frequency of 1050 Hz, and registers limbus of cornea and edge of a pupil. Both models are equipped with software for custom treatments. [167] (Table 2)

Star S4 IR (Abbot Medical Optics, Santa Ana, California, USA) – is a laser which beam has adjustable size of aiming spot that variates from 0,65 to 6,5 mm. Laser works on a frequency of 10/20 Hz, and has incorporated 3D iris recognition eye tracking system with speed of 60 Hz. Software program of the laser enables custom treatments also. [168, 169] (Table 2)

Technolas 217z (Bausch & Lomb, Rochester, New York, USA) – laser that works with speed of 100 Hz with laser beam of truncated Gaussian profile and size of aiming spot of 2 mm. Thermal damage of corneal surface is controlled with overlapping form of aiming spots. It has 6D eye tracking system incorporated founded on iris recognition, and compensates movements on x/y/z axis, static and dynamic cyclotorsion, and iris movements. Software program besides custom treatments enables treatment of presbyopia with “Supracor” method. [170-172] (Table 2)

Nidex Quest/EC-5000 CX III (Nidek CO Ltd, Gamagori, Japan) – is “scanning slit laser” which cuboid beam is divided into six equal aiming spots with 1 mm size Gaussian profile. Laser works on 100 Hz frequency and has incorporated 6D eye tracking system, speed of 1 kHz. Software program enables custom ablations. [173] (Table 2)

TABLE 2. Display of basic characteristics of excimer lasers available on the market

CHARACTERISTICS	WAVELIGHT EX500	SCHWIND AMARIS 1050	MEL 90	STAR S4 IR (VISX)	TECHNOLAS 217P	NIDEK Quest/EC-5000 CX III
Type of ablation	“Flying spot“	“Flying spot“	“Flying spot“	Adjustable spot size	“Flying spot“	“Scanning slit“
Beam profile	Ultra-thin Gaussian profile	Super Gaussian Profile	Gaussian Profile	Gaussian Profile	Truncated Gaussian profile	Gaussian Profile
Spot size (mm)	0,68	0,54	0,7	0,65-6,5	1-2	1
Pulse frequency (Hz)	500	1050	250/500	10-20	100	100
Speed of eye tracking system (Hz)	1050	1050	1050	60	240	200/1000
Characteristics of eye tracking system	6D tracking system	7D tracking system	Registration of pupil edge and limbus	3D tracking system	6D tracking system	6D tracking system

2. HYPOTHESIS

Schwind Amaris 750S provides superior refractive results when treating high astigmatism compared to Wavelight Allegretto Eye-Q. Aberration free program of Schwind induces less high order aberrations (HOAs) than Wavelight optimized treatment.

3. AIMS OF THE RESEARCH

1. To analyse functional parameteres after performed LASIK- uncorrected (UDVA) and corrected distant visual acuity (CDVA), residual refractive error, astigmatism outcomes by means of vector analysis and high order aberrations in patients with high astigmatism (more than 2 diopters (D)) treated with Wavelight Allegretto Eye-Q laser platform.

2. To analyse functional parameters after performed LASIK- uncorrected (UDVA) and corrected distant visual acuity (CDVA), residual refractive error, astigmatism outcomes by means of vector analysis and high order aberrations in patients with high astigmatism (more than 2 diopters (D)) treated with Schwind Amaris 750S laser platform.

3. To investigate the differences in uncorrected distant visual acuity (UDVA) in patients treated with two different excimer laser platforms.

4. To investigate the differences in corrected distant visual acuity (CDVA) in patients treated with two different excimer laser platforms.

5. To investigate the differences in residual refractive error in patients treated with two different excimer laser platforms.

6. To determine the significance in the astigmatism outcomes by means of vector analysis in patients treated with two different excimer laser platforms.

7. To investigate the differences in high order aberrations in patients treated with two different excimer laser platforms.

4. PATIENTS AND METHODS

4.1. PATIENTS

Research was performed at University Eye Hospital Svjetlost in Zagreb, Croatia. Patients were included between January 2010 and December 2011, and had a follow up of one year. During the inclusion period 3503 patients were examined for laser eye surgery at the Cornea and Refractive Surgery Department. Out of 3503 patients, 1020 patients were not suitable for excimer laser surgery because of their high refractive error and/or inadequate ratio of refractive error and corneal thickness, which was out of the safety limit for the laser eye surgery (163 patients), plano presbyopic patients or combination of refractive errors – myopia/ hypermetropia with presbyopia (572 patients), lens opacities (118 patients), irregularities of the cornea and/or ectatic corneal diseases (60 patients), retinal problems (45 patients), injuries of the eye (34 patients) and newly discovered glaucoma patients (28 patients).

Out of 2483 patients, PRK method was recommended for 350 of them. Out of 2183 patients who were suitable for LASIK 274 patients who met the criteria were included in the study.

Two hundred and seventy-four patients (470 eyes) with astigmatism more than 2 diopters (D) were operated and two hundred and thirty seven patients (418 eyes) completed one year of follow-up. Operation was performed on two hundred and seventy four patients (274) instead of planned two hundred sixty (260) patients needed for the study, taking into account that some patients can be lost in the follow up period. Exactly that situation occurred. Two hundred and thirty-seven (237) patients actually made visits for control examinations, but that number is less than percentage allowed in the proposal, so data of the research is valid (up to 15% loss of patients is considered allowed for needed data of this research).

The inclusion criteria were: patients over 18 years of age with a refractive error stable for at least one year, astigmatism ≥2.0 D, corneal thickness ≥500 micrometers (μm), mesopic pupil ≤7.5 millimeters (mm), and unremarkable corneal topography. Patients with peripheral retinal degeneration were evaluated by specialists and subjected to argon photocoagulation before the refractive procedure when indicated.

Exclusion criteria were topographic patterns that were suggesting any form of ectatic corneal disease, and systemic or ocular diseases that could interfere with the healing process of the cornea. Patients with previous ocular surgery were also excluded.

Patients were separated into two groups according to the laser platform on which they were treated – Wavelight Allegretto Eye-Q 400 Hz and Schwind Amaris 750S. Within each group, the treated eyes were further subdivided according to the type of astigmatism, myopic astigmatism or mixed astigmatism. A total of 188 eyes (110 patients) were included in the Allegretto group. There were 127 eyes (71 patients) with myopic astigmatism and 61 eyes (39 patients) with mixed astigmatism. A total of 230 eyes (127 patients) were included in the Amaris group. There were 119 eyes (64 patients) with myopic astigmatism and 111 eyes (63 patients) with mixed astigmatism.

4.2. METHODS

4.2.1. PREOPERATIVE EXAMINATION

Every patient had complete preoperative ophthalmologic examination prior to deciding if the patient met the criteria for corneal refractive surgery. Examination included uncorrected and corrected distant visual acuity (UDVA, CDVA), manifest and cycloplegic refraction, corneal topography measured on pentacam (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany), aberrometry (L 80 wave+, Luneau SAS, Prunay-le Gillon, France), tonometry (Auto Non-Contact Tonometer, Reichert Inc., Buffalo, NY, USA), slit-lamp and dilated funduscopic examination. Visual acuity was measured using a standard Snellen acuity chart at 6 m and presented in decimal format. The patients were asked to discontinue use of contact lenses for up to 4 weeks prior to this examination, depending on the type of lenses they were using.

Patients with stable refraction, astigmatism ≥2.0 D, regardless of the amount of myopic or hyperopic spherical correction, were included. Ocular criteria were those normally adopted in refractive surgery. Patients with history of ocular surgery, abnormal corneal topography, preoperative corneal thickness <490 μm or calculated residual stromal bed thickness <280 μm were excluded from the study.

4.2.2. VISUAL ACUITY MEASUREMENT

Uncorrected and corrected distant visual acuity were measured on a digital screen (Clear Chart 4 Digital Acuity, Reichert Technologies, Buffalo, New York, USA). For testing Snellen chart with Sloans letters was used. The chart has letters of different sizes arranged from largest at the top to smallest at the bottom, which are read, one eye at a time, at a distance of 6 meters (20 feet). Each letter on the chart subtends an angle of 5 minutes (min) of arc at the appropriate testing distance, and each letter part subtends an angle of 1 min of arc. Thus, it is designed to measure acuity in angular terms. Snellen acuities are usually expressed as a fraction with the numerator equal to the distance from the chart and the denominator being the size of the smallest line that can be read. The reciprocal of the fraction equals the angle, in min of arc, that the stroke of the letter subtends on the patient's eye and is called the minimum angle of resolution (MAR).

For maximal visual acuity the row in which patients did not see and/or misread maximum two letters – was recorded (entered); in the case where there was larger number of misread letters visual acuity of previous row was taken into account. Visual acuity was expressed as a decimal that is equal to the numeric value of the Snellen fraction or the reciprocal of the visual angle in minutes, so 20/20 would become 1.0. [174]

4.2.3. HIGH ORDER ABERRATIONS MEASUREMENT

Total ocular high order aberrations were evaluated – coma, trefoil and spherical aberrations. Measurements were performed by Luneau Visionix L 80 Wave+ aberrometer, based on Hartman Shack sensor (Visionix, Prunay-le-Gillon, France).

Measurements were performed on native narrow pupil after 10 minutes adaptation in the dark (5mm). Values of coma were used as a root mean square (RMS) of quadrant coefficient Z-13 and Z 13 values addition, trefoil values were used as a root mean square (RMS) of quadrant coefficient Z-33 and Z 33 values addition. Values of spherical aberrations were taken as amount of Z 04 coefficient.

4.2.4. SURGICAL TECHNIQUE

Prior to the surgery, two drops of topical anesthetic (Novesine, OmniVision GmbH, Puchheim, Germany) were instilled at 2 minute intervals (care should be taken to ensure that the drops are not instilled too early, as doing so may loosen the epithelium substantially), and the eye was cleaned with 2.5% povidone iodide. First, procedure was performed on the right eye. When it was completed, the same procedure was repeated on the left eye. After the patient was positioned under the laser, a sterile drape was placed over the upper eyelid skin and eyelashes. An eyelid speculum was placed in the eye to be treated, and an opaque patch was placed over the fellow eye to avoid cross-fixation. A gauze pad was taped over the temple between the eye to be treated and the ear on that side – to absorb any excess fluid. The patient was asked to fixate on the green laser centration light. It is important for the plane of the eye to remain parallel to the plane of the laser, for the patient to maintain fixation, and for the surgeon to control centration even when using lasers with tracking systems (both lasers in this research have eye tracking systems). For most patients, voluntary fixation during photoablation produces more accurate centration than globe immobilization by the surgeon.

Before creating the flap asymmetric sterile ink marks in the corneal periphery were made, positioned at 3 and 9 o'clock away from the intended flap hinge. These marks can aid in alignment of the flap at the end of the surgery. Eye was fully irrigated with balanced salt solution and the excess liquid was dried out afterwards with the Merocel surgical microsponges (Medtronic, Jacksonville, FL, USA). A corneal flap was created using Moria M2 mechanical microkeratome with 90 μm head (Moria, Antony, France). The microkeratome was sterilized and assembled by technical personnel and tested by the surgeon before each operation.

After the removal of excess liquid, metal ring of microkeratome was placed on the eye. The microkeratome head was engaged into the suction ring and then moved over the cornea with a purpose of creating flap with 8,5-9,0 mm in diameter (size of the ring was chosen according to the nomogram depending on keratometric values), and then vacuum was applied. When adequate vacuum of 150 mm was accomplished, microkeratome motor with previously assembled 90 μm blade was placed on the ring. Blade of 90 μm is predicted for creation of 110 μm flap (during the use of speed 1 on Evolution 3 central unit). With a use of automatic foot pedals, microkeratome was driven over the eye with the goal of a superior hinge formation. After the flap creation, complete unit – consisted of vacuum ring and motor – was lifted from the eye, and inspection of flap quality was performed. Then, with a help of the LASIK spatula flap was lifted and moved to 12o'clock position on the superior conjuctiva. Corneal stroma was dried from the excess liquid with a triangle microsponge, and excimer laser ablation was applied.

Either Wavelight Allegretto Eye-Q 400 Hz (Alcon, Forth Worth, TX, USA) or Schwind Amaris 750S (Schwind eye-tech-solutions, Kleinostheim, Germany) were used for the excimer laser treatment. Wavelight Allegretto is a scanning spot laser with Gaussian beam profile and beam size of 0.95 mm. Average fluence is 200 (mJ/cm²). Schwind Amaris 750S is a scanning spot laser with Super Gaussian beam profile and beam size of 0.54 mm.

Average fluence is automatic; depending on the planned refractive correction, approximately 80% of the corneal ablation is performed with a high fluence level (>400 mJ/cm²) and this leads to a considerable reduction in time spent treating the cornea. Fine correction is performed for the remaining 20% of the treatment using a low fluence level (<200 mJ/cm²), aimed to reduce the amount ablated per pulse and smooth out the ablated stromal bed.

In all patients treated with Allegretto Eye-Q laser, the optical zone was fixed at 6.5 mm as recommended by the manufacturer, and the wavefront optimized program was used. Since the laser ablation algorithm is based on preservation of corneal asphericity by delivering additional laser pulses on the periphery to maintain a natural corneal shape, total ablation zones were wide; 8.9 for mixed astigmatism and 9.0 mm for myopic astigmatism cases. For the Amaris 750S, the mean optical zone of the treatment was 6.63±0.20 mm (range 6.5 to 7.0 mm). The rationale for changing optical zone was based on the manufacturer's recommendation to select, at least, a 6.7 mm optical zone for treatment of astigmatism. However, the goal was not to exceed 9.0 mm zone of total ablation. Since the transition zone (automatically calculated by the system for the selected optical zone and applied correction) increases with the complexity of the applied correction, size of an optical zone was chosen to fit within the limits of 9.0 mm of total ablation zone. The total ablation zone was 8.67±0.31 mm (range 7.9 to 9.0 mm). The Aberration FreeTM program was applied in all cases. All ablations were centered on corneal vertex for both laser platforms. The corneal vertex is the intersection of the papillary axis with the anterior surface of the cornea, when the pupillary axis coincides with the optical axis of the measuring device. [175]

The position of the corneal vertex was determined by the pupillary offset, that is the distance between the pupil center and the normal corneal vertex,[176] calculated by using the videokerato-scope (CSO, Costruzione Strumenti Oftalmici, Florence, Italy) for Amaris, and Scheimpflug camera (Pentacam HRTM, Oculus Optikgeräte GmbH, Wetzlar, Germany) for Allegretto. The Cartesian coordinates of the corneal vertex were manually entered into the software program. [176]

For all patients, the programmed treatment consisted of cycloplegic spherical correction with manifest astigmatic power and axis. For the Allegretto Eye-Q, the "Wellington nomogram" provided by the company was used for spherical correction. The nomogram also directs the surgeon to correct 25% less of the full astigmatism. Previous experience showed that the 25% modification led to significant undercorrection. Thus, it was decided to use an empirically derived undercorrection of 15% in all cases where the Allegretto Eye-Q was used. For the Amaris 750S the sphere, cylinder, and axis were entered into laser without nomogram adjust-ment. Before excimer laser ablation, proper alignment of the eye with Allegretto Eye-Q was achieved with a manual cross technique to compensate for cyclotorsion. The Allegretto Wave operates with closed-loop 3D eye tracker of 400 Hz implyng rate, with automatic pupil centering. It has an integrated cross-line projector for alignment of the head and eye position, with a "NeuroTracker" for cyclotorsion control for the wavefront-optimized algorithm. Its eye-tracker system and laser trigger are synchronized. [177]

Schwind Amaris 750S features a six-dimensional 1050 Hz infrared eye tracker with simultaneous limbus, pupil, iris recognition, and cyclotorsion tracking integrated in the laser delivery process.

The built-in 6D eye tracker automatically compensated for static and dynamic cyclotorsion of the eye.

In all cases, the flap was lifted and excimer laser ablation was delivered to the stroma. Patients were instructed to concentrate on the fixation light throughout the ablation. When the ablation with excimer laser was completed, the eye, specially the interface was irrigated with balanced salt solution, removing any debris and flap was repositioned on the stroma. Edges of the flap were carefully dried with the use of triangular microsponge. After the final inspection of the flap position, combination of antibiotic and steroid drops were instilled into the eye, and the eyelid speculum and sterile drape were gently removed.

TABLE 3. The main differences between the two laser platforms

	SCHWIND AMARIS 750S	WAVELIGHT ALLEGRETTO 400 Hz
Ablation type	Scanning spot	Scanning spot
Beam profile	Super Gaussian	Gaussian
Beam size (mm)	0.54	0.95
Average fluence (mJ/cm2)	Automatic (faster-slower)	200
Pulse frequency	750	400
Eye tracker implying rate (Hz)	1050	400
Cyclotorsion compensation	YES Static and dynamic	NO
Optical zone	ADJUSTABLE	CONDITIONAL FIXED 6.5mm

4.2.5. POSTOPERATIVE THERAPY

Postoperative therapy included combination of topical antibiotic and steroid drops (Tobradex, Alcon, ForthWorth, TX, USA) 4 times daily for 10 days, and artificial tears (Blink, Abbott Medical Optics, Santa Ana, CA, USA) 6–8 times daily for at least 1 month.

4.2.6. POSTOPERATIVE EVALUATION

All patients were examined 1 day, 1 week, 1 month, 3 months, and 1 year after the surgery. Evaluation included measurement of UDVA, CDVA, manifest refraction, aberrometry, slit-lamp examination, tonometry, and corneal topography. Results at 1 year postop were also used to perform the vector analysis and statistical evaluation.

4.2.7. VECTOR ANALYSIS

Astigmatism is measured by its magnitude and axis. These two values must be considered together. Consequently, it is difficult to perform even the simpliest statistical analysis of refractive data. With that reason vectors were used, they incorporate magnitude and axis, two data into one.

4.2.7.1. THIBOS METHOD

The method [178] implies application of Fourier analysis to describe the sinusoidal variation of power in the astigmatic refraction. [178-181]

According to this method, astigmatism was converted from the spherocylinder notation (units of diopter) to a single point in a 3 – dimensional dioptric space, called *power vector* notation. The first component is a spherical lens with power M equal to the spherical equivalent of the given refractive error (S = sphere + cylinder/2). The remaining two components come from a Jackson crossed cylinder, equivalent to a conventional cylinder of positive power J at axis α + 90° (α = the meridian of maximum positive power or angle of astigmatic prescription) crossed with a cylinder of negative power -J at axis 90°. Thus, a power vector is that vector drawn from the coordinate origin of this space to the point (S, J_0, and J_{45}). [180, 181]

The magnitude of the astigmatic power vector (APV) on the astigmatic plane is defined by (J_0 2 +J_{45} 2) 1/2 and represents a non-signed scalar that may be used to determine statistical differences in the magnitude of astigmatism between two datasets. [182-186]

J_0 refers to cylinder power set at orthogonally 90° and 180° meridians, representing Cartesian astigmatism.

Positive values of J_0 indicate WTR astigmatism and negative values of J_0 indicate ATR astigmatism.

J_{45} refers to a cross-cylinder set at 45° and 135°, representing oblique astigmatism.

$$J_0 = \left(\frac{cylinder}{2}\right) \times \cos\left[\frac{4\pi(\emptyset-90)}{360}\right]$$

$$J_{45} = \left(\frac{cylinder}{2}\right) \times \sin\left[\frac{4\pi(\emptyset-90)}{360}\right]$$

$$M = \text{sphere} + \left(\frac{cylinder}{2}\right)$$

4.2.7.2. ALPINS METHOD

The Alpins Method, developed by Australian ophthalmologist Noel Alpins, is a system to plan and analyse the results of refractive surgical procedures, such as LASIK. [187-189]

The Alpins Method uses vector mathematics to determine a goal for astigmatism correction and analyse factors involved if treatment fails to reach that goal. The method can also be used to refine surgical techniques or correct laser settings in future procedures. [190]

The Alpins method is a vectorial analysis that allows determination of the effectiveness of a specific astigmatic treatment. It considers both magnitude and orientation of astigmatism. Three fundamental vectors are used in the analysis: target-induced astigmatism (TIA) – the astigmatic change the surgery was intended to induce, surgically induced astigmatism (SIA) – the astigmatic change the surgery actually induced and difference vector (DV) – the induced astigmatic change that would enable the initial surgery to achieve its intended target. Various relationships between these vectors, such as correction index (SIA/TIA), flattening index ([SIA x Cos 2 x angle between SIA and TIA]/TIA), index of success (DV/TIA) among others, provide a complete description of the astigmatic correction achieved with a specific modality of treatment. It can be determined whether the treatment was on axis, or off axis and whether too much, or too little effect was achieved. [190]

4.3. STATISTICAL ANALYSIS

Data were analysed to determine significance of change in spherical correction, astigmatism, UDVA, CDVA, high order aberrations, (z-test, 2 – Sample Assuming Unequal Variances for data with normal distribution and Mann-Whitney U test for non-parametric analysis) within each group and between groups to determine whether there was significant difference between two lasers. Changes and differences were considered statistically significant when $p<0.05$. Spherical aberration was further analysed with cluster analysis to see the trend in change.

Data were further analysed with Pearson correlation to determine the significance of any correlation between pre and postoperative sphere, cylinder and visual acuity. Correlations were considered significant when $p<0.05$.

Refractive cylinder data were further analysed with Thibos method. The J_0 and J_{45} vectors were calculated for the refractive data collected preop and at 1 year postoperative. Cases were separated into 4 groups as follows:

Group 1, myopic astigmatism treated with Allegretto (n=127 eyes)
Group 2, myopic astigmatism treated with Amaris (n=119 eyes)
Group 3, mixed astigmatism treated with Allegretto (n=61 eyes)
Group 4, mixed astigmatism treated with Amaris (n=111 eyes)

The data were analysed to determine the significance of any:

1. Difference in the means between the two groups of myopic astigmatic cases both before and after treatment according to the two astigmatic vectors J_0, and J_{45} (t test).
2. Difference in the means between the two groups of mixed astigmatic cases both before and after treatment according to the two astigmatic vectors J_0, and J_{45} (t test).
3. Correlation between the change (Δ) in each astigmatic vector (J_0 and J_{45}) and pretreatment astigmatic vector value within each of the four groups (Pearson correlation) and apparent difference between the two correlation coefficients, for each of the two platforms, within four groups (Fischer's 'r' to 'z' transformation).
4. Association between J_0 and J_{45} vectors before and after treatment within each of the 4 groups (Pearson correlation).

The null hypothesis was rejected when p exceeded 0.01.

In addition, refractive cylinder data were also analysed with Alpins method.

The data were analysed as follows:

1. To determine if the surgically induced astigmatic power and axis was significantly correlated with the target induced astigmatic power (Pearson correlation coefficient, r multiple linear regression).
2. To determine if the surgically induced astigmatic axis was significantly correlated with the target induced astigmatic power and axis (Pearson correlation coefficient, r multiple linear regression).
3. To determine the significance of any association between ΔC (the difference between the surgically induced astigmatic power minus the target induced astigmatic power) and the target induced astigmatic power.
4. To determine the significance of any association between Δθ (the difference between the surgically induced astigmatic axis minus the target induced astigmatic axis) and the target induced astigmatic axis.
5. To determine the significance of any apparent differences of average Δθ values between platforms.

The significance level was set at a $p<0.05$.

4.4. ETHICAL ASPECTS OF RESEARCH

Described research assured compliance of basic ethical and bioethical principles – personal integrity (autonomy), equity, benevolence and safety – in accordance with Nurnberg code and newest revision of the tenets of the Helsinki agreement. Medical data was collected according to ethical and bioethical principles, and privacy of the patients included in research (medical secret) was assured together with secrecy.

The study was approved by the Ethics Committee of University Eye Hospital Svjetlost Zagreb, Croatia. All patients signed detailed preoperative informed consent after they received an explanation of the procedure, including all risks and benefits of the proposed treatment together with possibilities of other, including non-surgical, astigmatism treatments.

5. RESULTS

5.1. VISUAL ACUITY

5.1.1. MYOPIC ASTIGMATISM

There was no statistically significant difference (*p*>0.05) in preoperative UDVA and CDVA between the patients from group 1 – Myopic astigmatism corrected with Wavelight Allegretto Eye-Q or group 2 – Myopic astigmatism corrected with Schwind Amaris 750S platform.

TABLE 4. Visual results of group 1 – Myopic astigmatism corrected with Wavelight Allegretto Eye-Q platform

Visual results – myopic astigmatism			
Wavelight Allegretto Eye-Q			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	0.15±0.15 (0.01 to 0.70)	0.86±0.16 (0.35 to 1.00)	<0.001
CDVA	0.81±0.17 (0.30 to 1.00)	0.89±0.16 (0.40 to 1.00)	<0.001

In the group 1, there was a statistically significant improvement in both postoperative UDVA and CDVA in comparison to preoperative results. (Table 4)

Values of postoperative UDVA showed improvement in comparison to preoperative CDVA. The difference was equivalent to half a line of Snellen letters and this was statistically significant (*p*=0.017). None of the eyes lost any lines of CDVA.

TABLE 5. Visual results of group 2 – Myopic astigmatism corrected with Schwind Amaris 750S platform

Visual results – myopic astigmatism			
Schwind Amaris 750S			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	0.13±0.11 (0.01 to 0.45)	0.86±0.19 (0.15 to 1.00)	<0.001
CDVA	0.81±0.18 (0.10 to 1.00)	0.89±0.20 (0.40 to 1.00)	0.001

In the group 2, there was a statistically significant improvement in both postoperative UDVA and CDVA in comparison to preoperative results. (Table 5)

Values of postoperative UDVA appear to show an improvement in comparison to preoperative CDVA.

The difference was not statistically significant (*p*=0.06). None of the eyes lost any lines of CDVA.

There was no difference in postoperative UDVA or CDVA between lasers for myopic astigmatism (*p*>0.05).

5.1.2. MIXED ASTIGMATISM

There was no statistically significant difference (*p*>0.05) in preoperative UDVA and CDVA between the patients from group 3 – Mixed astigmatism corrected with Wavelight Allegretto Eye-Q and patients from group 4 – Mixed astigmatism corrected with Schwind Amaris 750S platform.

TABLE 6. Visual results of group 3 – Mixed astigmatism corrected with Wavelight Allegretto Eye-Q platform

Visual results – mixed astigmatism			
Wavelight Allegretto Eye-Q			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	0.25±0.14 (0.03 to 0.60)	0.77±0.20 (0.20 to 1.00)	<0.001
CDVA	0.74±0.22 (0.15 to 1.00)	0.82±0.21 (0.20 to 1.00)	0.04

In the group 3 there was a statistically significant improvement in both postoperative UDVA and CDVA in comparison to preoperative results. (Table 6)

Values of postoperative UDVA appear to show an improvement in comparison to preoperative CDVA but this was not statistically significant (*p*>0.05). None of the eyes lost any lines of CDVA.

TABLE 7. Visual results of group 4 – Mixed astigmatism corrected with Schwind Amaris 750S platform

Visual results – mixed astigmatism			
Schwind Amaris 750S			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	0.24±0.12 (0.02 to 0.60)	0.80±0.21 (0.05 to 1.00)	<0.001
CDVA	0.77±0.20 (0.04 to 0.95)	0.85±0.21 (0.10 to 1.00)	0.04

In the group 4, there was a statistically significant improvement in both postoperative UDVA and CDVA in comparison to preoperative results. (Table 7)

Values of postoperative UDVA show an improvement in comparison to preoperative CDVA. The difference was not statistically significant (*p*>0.05). None of the eyes lost any lines of CDVA.

There were no differences between UDVA and CDVA for mixed astigmatism.

5.2. REFRACTIVE RESULTS

5.2.1. MYOPIC ASTIGMATISM

There was no statistically significant difference (*p*>0.05) in preoperative sphere or cylinder between the patients from group 1 – Myopic astigmatism corrected with Wavelight Allegretto Eye-Q and patients from group 2 – Myopic astigmatism corrected with Schwind Amaris 750S platform.

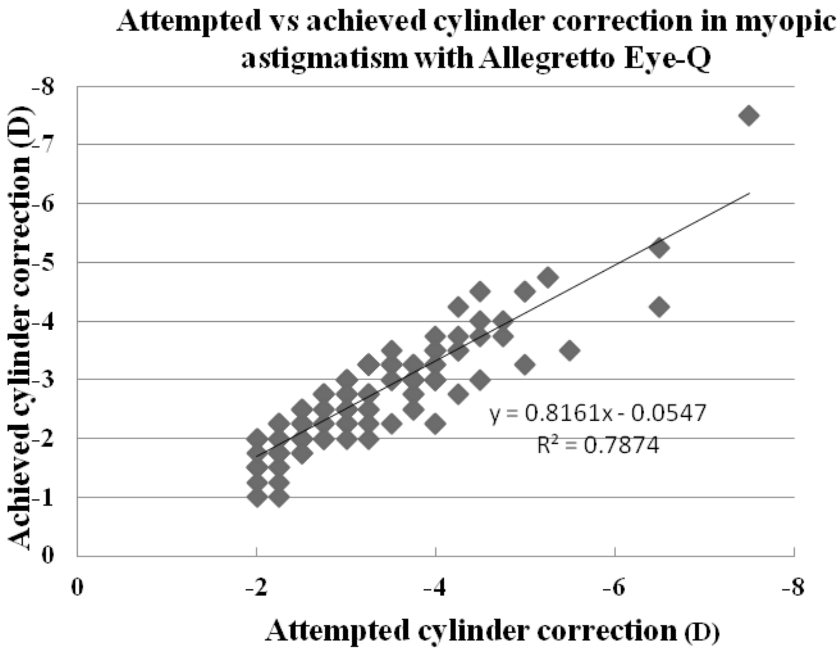
TABLE 8. Refractive results of group 1 – Myopic astigmatism corrected with Wavelight Allegretto Eye-Q platform

Refractive results - myopic astigmatism			
Wavelight Allegretto Eye-Q			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	-2.80±2.01 (-8.50 to 0.00)	-0.16±0.46 (-1.50 to +1.00)	<0.001
CDVA	-3.30±1.00 (-7.50 to -2.00)	-0.55±0.46 (-2.25 to 0.00)	<0.001

In the group 1, average sphere decreased from −2.80 D to −0.16 D (*p*<0.001), and average cylinder decreased from −3.30 D to −0.55 D (*p*<0.001).

There was a statistically significant shift towards zero (i.e. emmetropia) in both postoperative sphere and cylinder in comparison to preoperative values.

FIGURE 12. Attempted vs. achieved cylinder correction of group 1 – Myopic astigmatism corrected with Allegretto Eye-Q platform



Attempted vs achieved cylinder correction (D) in myopic astigmatism corrected with Allegretto Eye-Q. The least-squares regression line, best-fit linear equation and R^2 are included for comparison with Figures 13, 14, & 15.

There was a highly significant association between the attempted and achieved astigmatic correction (R^2=0.7874).

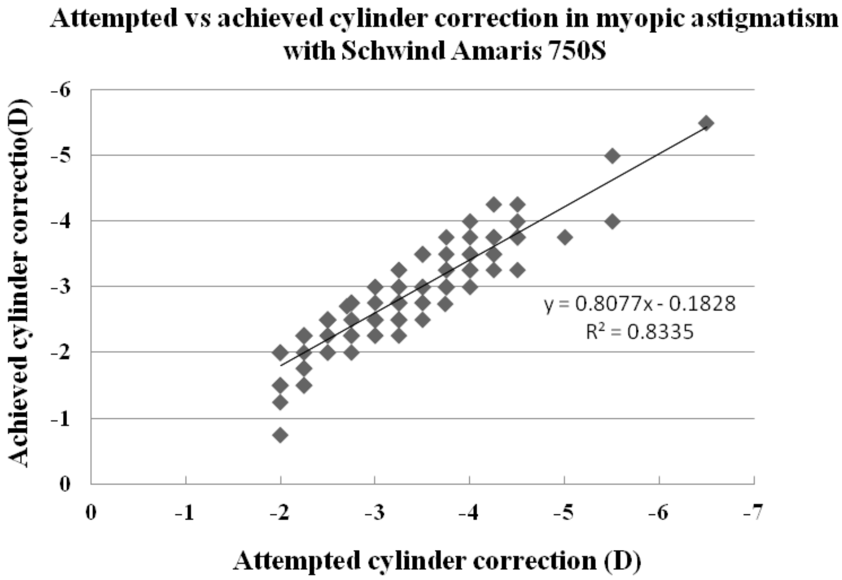
TABLE 9. Refractive results of group 2 – Myopic astigmatism corrected with Schwind Amaris 750S platform

Refractive results – myopic astigmatism			
Scwind Amaris 750S			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	-2.44±2.17 (-7.50 to 0.00)	-0.16±0.55 (-2.00 to +1.25)	<0.001
CDVA	-3.21±0.87 (-6.50 to -2.00)	-0.43±0.36 (-1.50 to 0.00)	<0.001

In the group 2, average sphere decreased from −2.44 D to −0.16 D ($p<0.001$) and average cylinder decreased from −3.21 D to −0.43 D ($p<0.001$).

There was a statistically significant improvement, shift towards zero (i.e. emmetropia) in both postoperative sphere and cylinder when comparing to preoperative values of sphere and cylinder.

FIGURE 13. Attempted vs. achieved cylinder correction of group 2 – Myopic astigmatism corrected with Schwind Amaris 750S platform



Attempted vs. achieved cylinder correction (D) in myopic astigmatism corrected with Amaris 750S. The least-squares regression line, best-fit linear equation and R^2 are included for comparison with Figures 12, 14 & 15.

For the myopic astigmatism treated with Amaris platform there was a highly significant association between the attempted and achieved astigmatic correction (R^2=0.8335).

There was no difference in effectiveness of spherical correction between laser platforms (p=0.969). There was a significant difference in effectiveness of cylinder correction between the groups (p=0.027). In the group 1, there was a tendency toward residual cylinder when comparing the attempted cylindrical correction with the postoperative cylinder (r=0.3978, p<0.01, n=127). The group 2 had less residual astigmatism than the group 1, and the difference was significant (p=0.027). The attempted and achieved astigmatic corrections revealed highly significant association between the attempted and achieved astigmatic corrections. (Figure 12 and Figure 13)

5.2.2. MIXED ASTIGMATISM

There was no statistically significant difference (p>0.05) in preoperative sphere or cylinder between the group 3 – patients corrected with Wavelight Allegretto Eye-Q and group 4 – patients corrected with Schwind Amaris 750S platform.

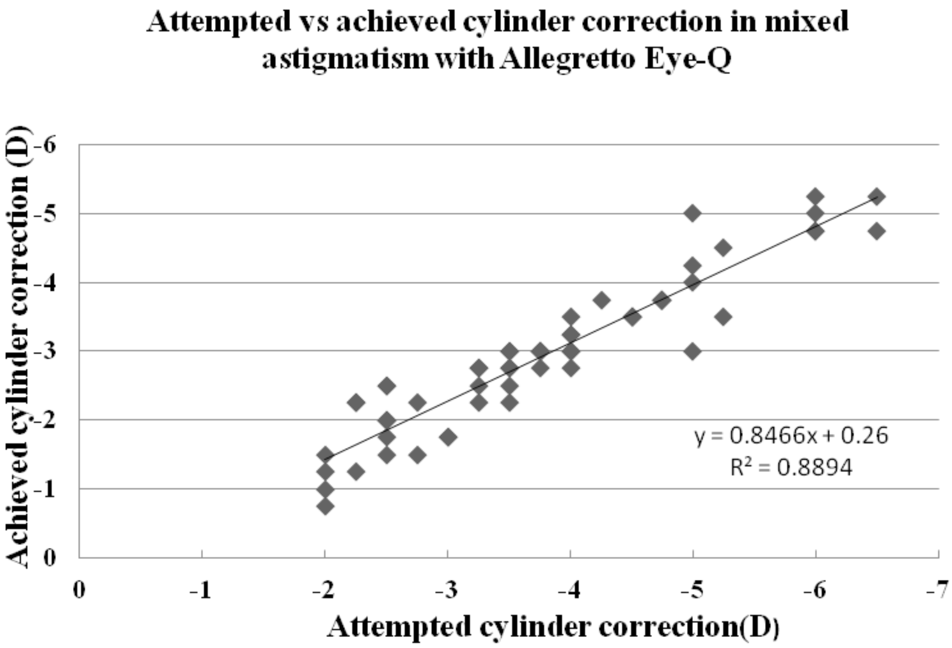
TABLE 10. Refractive results of group 3 – Mixed astigmatism corrected with Wavelight Allegretto Eye-Q platform

Refractive results - mixed astigmatism			
Wavelight Allegretto Eye-Q			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	2.72±1.79 (0.25 to 7.00)	0.19±0.52 (-1.50 to +1.50)	<0.001
CDVA	3.84±1.21 (-6.50 to -2.00)	-0.85±0.41 (-2.00 to 0.00)	<0.001

In the group 3, average sphere decreased from +2.72 D to +0.19 D (p<0.001). Average cylinder decreased from −3.84 D to −0.85 D (p<0.001).

There was a statistically significant shift towards zero (i.e. emmetropia) in both postoperative sphere and cylinder in comparison to preoperative values of sphere and cylinder.

FIGURE 14. Attempted vs. achieved cylinder correction of group 3 – Mixed astigmatism corrected with Wavelight Allegretto Eye-Q platform



Attempted vs. achieved cylinder correction (D) in mixed astigmatism corrected with Allegretto Eye-Q. The least-squares regression line, best-fit linear equation and R^2 are included for comparison with Figures 12, 13 & 15.

For the mixed astigmatism cases treated with Wavelight Allegretto Eye-Q there was a highly significant association between the attempted and achieved astigmatic correction (R^2=0.8894).

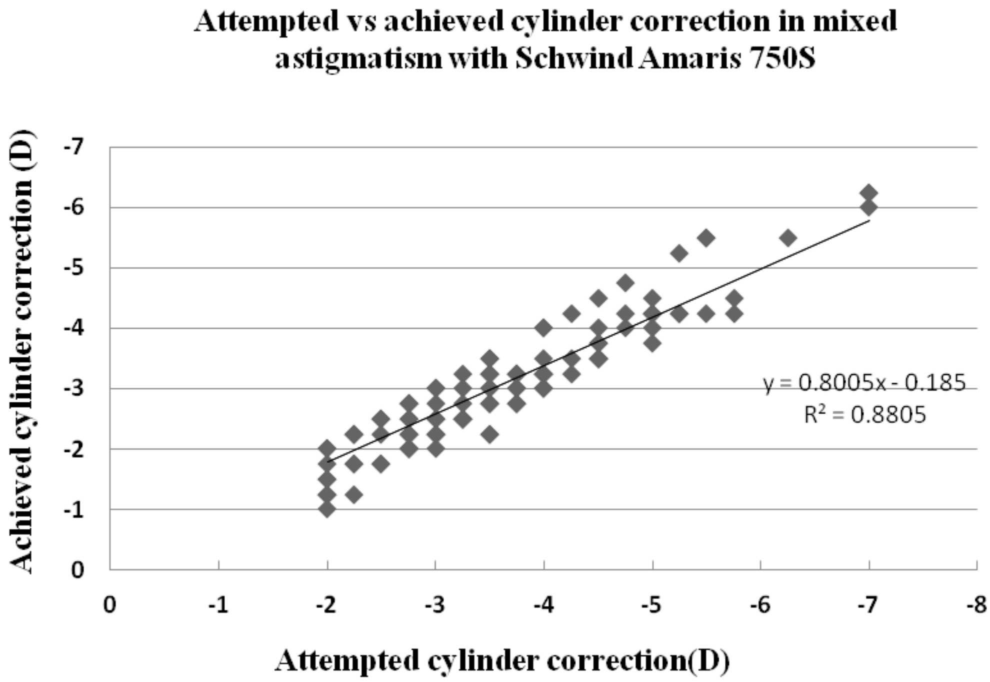
TABLE 11. Refractive results of group 4 – Mixed astigmatism corrected with Schwind Amaris 750S platform

Refractive results – mixed astigmatism			
Scwind Amaris 750S			
Variable	*Mean±standard deviation (range)*		
	Preop	*Postop*	*p value**
UDVA	3.11±1.57 (+0.50 to +7.50)	0.28±0.45 (-0.75 to +1.00)	<0.001
CDVA	-3.66±1.16 (-7.00 to -2.00)	-0.58±0.38 (-1.50 to 0.00)	<0.001

In the group 4, average sphere decreased from +3.11 D to +0.28 D (p<0.001) and average cylinder decreased from −3.66 D to −0.58 D (p<0.001).

There was a statistically significant shift towards zero (i.e. emmetropia) in both postoperative sphere and cylinder comparing to preoperative values of sphere and cylinder for mixed astigmatism treated with Amaris laser platform.

FIGURE 15. Attempted vs. achieved cylinder correction of group 4 – Mixed astigmatism corrected with Schwind Amaris 750S platform



Attempted vs achieved cylinder correction (D) in mixed astigmatism corrected with Amaris 750S. The least-squares regression line, best-fit linear equation and R^2 are included for com-parison with Figures 12,13 & 14.

For the Amaris 750s laser platform there was a highly significant association between the attempted and achieved astigmatic correction (R^2=0.8805).

There was no difference in effectiveness of spherical correction between laser platforms (*p*=0.236). There was a significant difference in effectiveness of cylinder correction between the groups (*p*<0.001). For the group 3, there was a tendency toward residual cylinder when comparing the attempted cylindrical correction with the postoperative cylinder (r=0.4567, *p*<0.01, n=61). The group 4 had less residual astigmatism than the group 3, and the difference was significant (*p*<0.001). The attempted and achieved astigmatic corrections revealed highly significant association between the attempted and achieved astigmatic corrections. (Figure 14 and Figure 15)

5.3. VECTOR ANALYSIS OF REFRACTIVE RESULTS

5.3.1. THIBOS METHOD

5.3.1.1. MYOPIC ASTIGMATISM

There was no statistically significant difference in preoperative mean values for J_0 and J_{45} between the groups (p=0.150, p=0.289) 1 and 2.

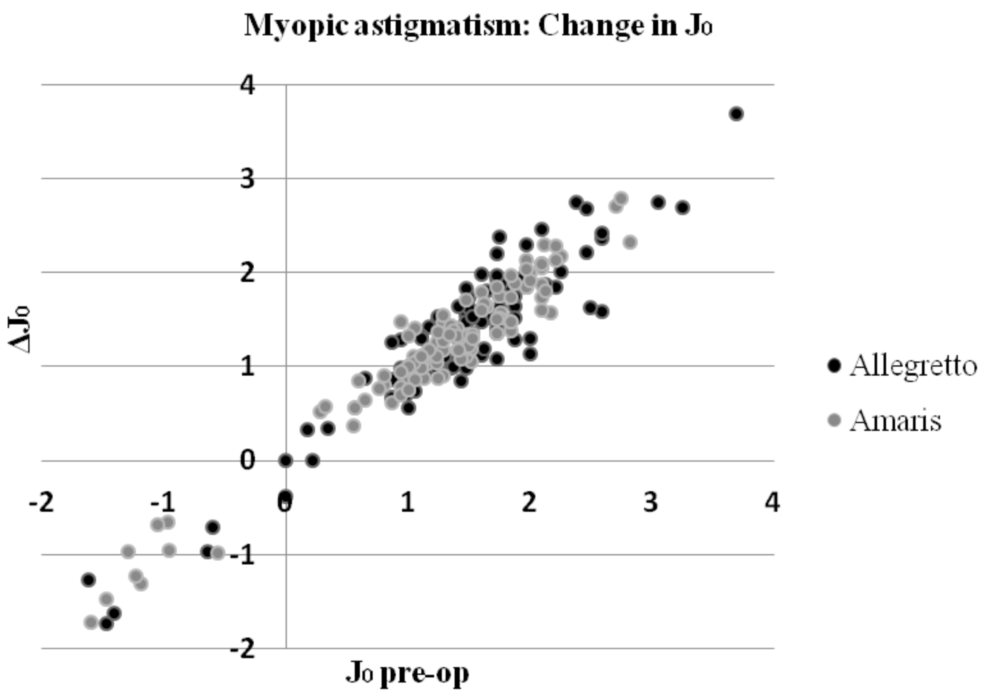
TABLE 12. Comparison of platforms for the J_0 and J_{45} vector (groups 1 and 2)

	Preop J_0	Postop J_0	*P*	Preop J_{45}	Postop J_{45}	*P*
	mean (± SD)	mean (± SD)		mean (± SD)	mean (± SD)	
Wavelight Allegretto Eye-Q	+1.369±0.776	+0.092±0.276	<0.001	+0.076±0.695	−0.058±0.204	0.042
Schwind Amaris 750S	+1.221±0.832	+0.065±0.202	<0.001	−0.023±0.769	+0.005±0.184	0.685
Comparison of platforms	p*=0.150	p*=0.380		p*=0.289	p*=0.012	

The J_0 and J_{45} vectors are defined in 4.2.7.1. in Methods section. The units of these vectors include trigonometric functions of angles (°) and dioptral power (D).

There was a statistically significant difference between J_0 preop and J_0 postoperatively for both platforms (p<0.001). There was no statistically significant difference for J_0 postoperatively between the platforms (p=0.380). There was no statistically significant difference between J_{45} preop and J_{45} postoperatively for either platform (p=0.042 and 0.685 for the Allegretto and Amaris groups respectively). There was a statistically significant difference for J_{45} postoperatively between the platforms (p=0.012). (Table 12)

FIGURE 16. Correlation between ΔJ_0 and preoperative J_0 values – comparison of platforms (groups 1 and 2)



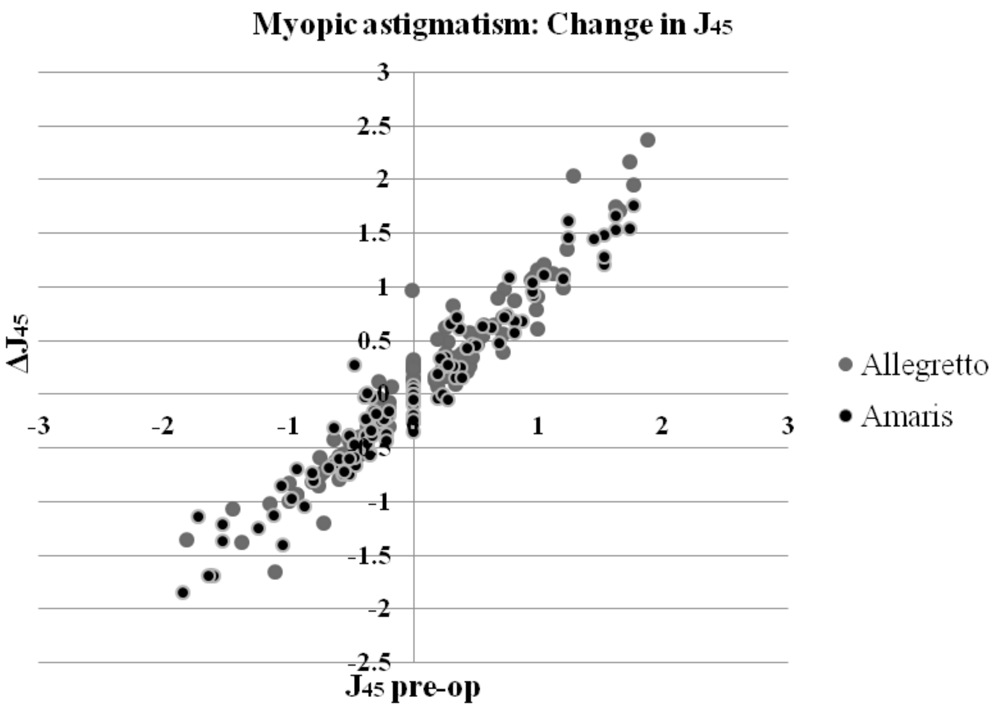
Comparison of the difference (Δ) between the pre- and postoperative J_0 vector values with preoper-ative J_0 values. The least squares regression lines equating ΔJ_0 and preoperative J_0 were as follows:

Group 1, ΔJ_0=0.924 ΔJ_0+0.190 (r=0.936, n=127, p<0.001).

Group 2, ΔJ_0=1.019 ΔJ_0+0.041 (r=0.971, n=119, p<0.001).

The difference between these two correlation coefficients was significant (z=−3.086, p=0.002).

FIGURE 17. Correlation between ΔJ_{45} and preoperative J_{45} values – comparison of platforms (groups 1 and 2)



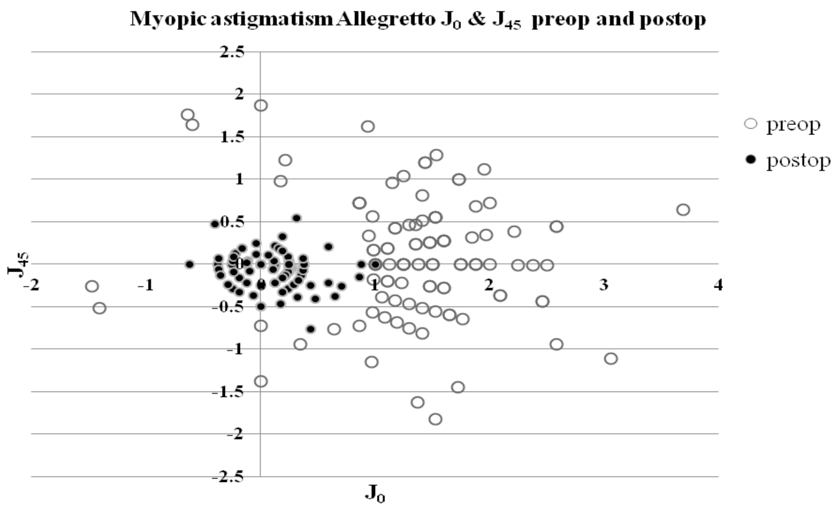
Comparison of the difference (Δ) between the pre- and postoperative J_{45} vector values with preoperative J_{45} values. The least squares regression lines equating ΔJ_{45} and preoperative J_{45} were as follows:

Group 1, ΔJ_{45}=0.905 ΔJ_{45} -0.046 (r=0.961, n=127, *p*<0.001).

Group 2, ΔJ_{45}=1.009 ΔJ_{45}+0.009 (r=0.971, n=119, *p*<0.001).

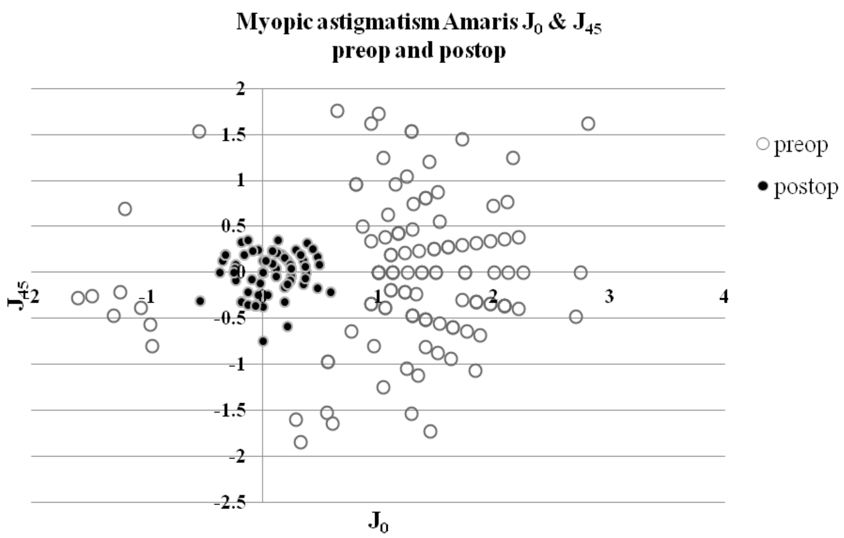
The difference between these two correlation coefficients was not significant (z=-1.13, *p*=0.259).

FIGURE 18. Association between pre- and postoperative values of J_0 and J_{45} for Wavelight Allegretto Eye-Q platform (group 1)



In the group 1, preoperative r=−0.158 (p=0.076) and postoperative r=−0.197 (p=0.026). Vector values are converging towards zero, but they are not zero. Treatments are working to nullify astigmatism but they don't cancel it out completely. Some residual astigmatism is still present after the surgery.

FIGURE 19. Association between pre- and postoperative values of J_0 and J_{45} for Amaris 750 S platform (group 2)



In the group 2, preoperative r=0.126 (p=0.172) and postoperative r=0.0904 (p=0.328). Vector values are converging towards zero, but they are not completely on the zero point. Some amount of residual astigmatism is still present after the surgery, so the treatments don't nullify all amount of astigmatism.

5.3.1.2. MIXED ASTIGMATISM

There was a statistically significant difference in preoperative mean values for J_0 (p<0.001) while there was no statistically significant difference in preoperative mean values for J_{45} (p=0.528) between the groups 3 and 4.

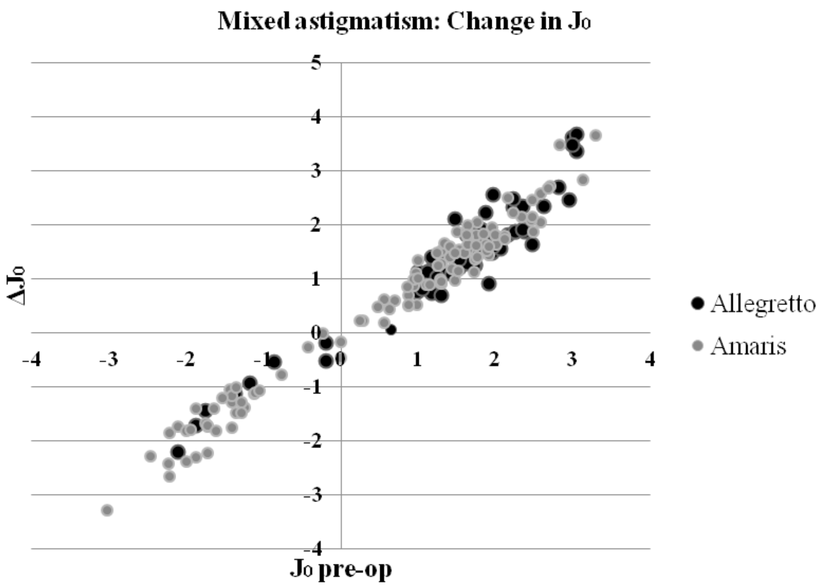
TABLE 13. Comparison of platforms for the J_0 and J_{45} vector (groups 3 and 4)

	Preop J_0 mean (± SD)	Postop J_0 mean (± SD)	*P*	Preop J_{45} mean (± SD)	Postop J_{45} mean (± SD)	*P*
Wavelight Allegretto Eye-Q	+1.417±1.198	+0.108±0.359	<0.001	−0.120±0.782	−0.039±0.285	0.424
Schwind Amaris 750S	+0.609±1.581	+0.064±0.268	<0.001	−0.036±0.916	−0.031±0.209	0.955
Comparison of platforms	p*<0.001	p*=0.402		p*=0.528	p*=0.863	

The J_0 and J_{45} vectors are defined in 4.2.7.1. in Methods section. The units of these vectors include trigonometric functions of angles (°) and dioptral power (D).

There was a statistically significant difference between J_0 preop and J_0 postoperatively for both platforms (p<0.001). There was no statistically significant difference for J_0 postoperatively between the platforms (p=0.402). There was no statistically significant difference between J_{45} preop and J_{45} postoperatively for either platform (p=0.424 and 0.955 for the group 3 and group 4 respectively). There was no statistically significant difference for J_{45} postoperatively between the platforms (p=0.863). (Table 13)

FIGURE 20. Correlation between ΔJ_0 and preop J_0 values – comparison of platforms (groups 3 and 4)



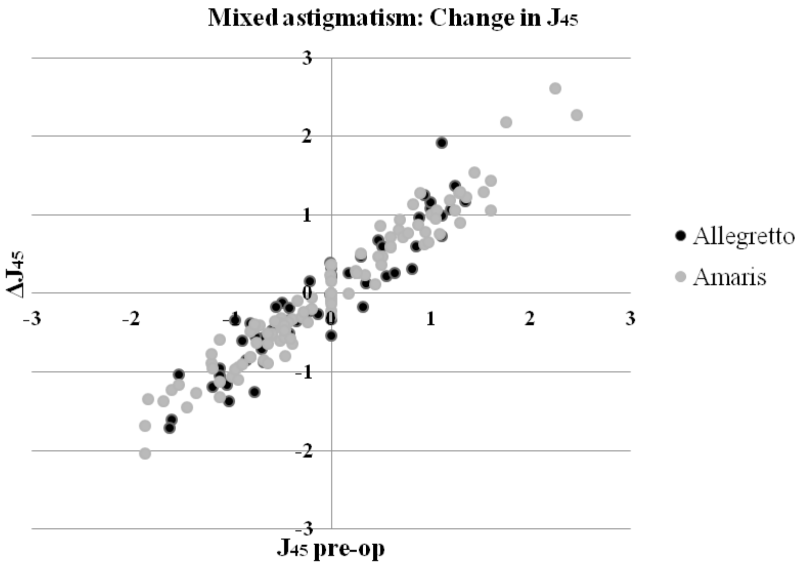
Comparison of the difference (Δ) between the pre- and postoperative J_0 vector values with preoperative J_0 values. The least squares regression lines equating ΔJ_0 and preoperative J_0 were as follows:

Group 3, $\Delta J_0 = 0.955\ J_0 + 0.168$ (r=0.955, n=61, p<0.001).

Group 4, $\Delta J_0 = 0.999\ J_0 + 0.065$ (r=0.986, n=111, p<0.001).

The difference between these two correlation coefficients was significant (z=−3.533, p=0.0004).

FIGURE 21. Correlation between ΔJ_{45} and preop J_{45} values – comparison of platforms (groups 3 and 4)



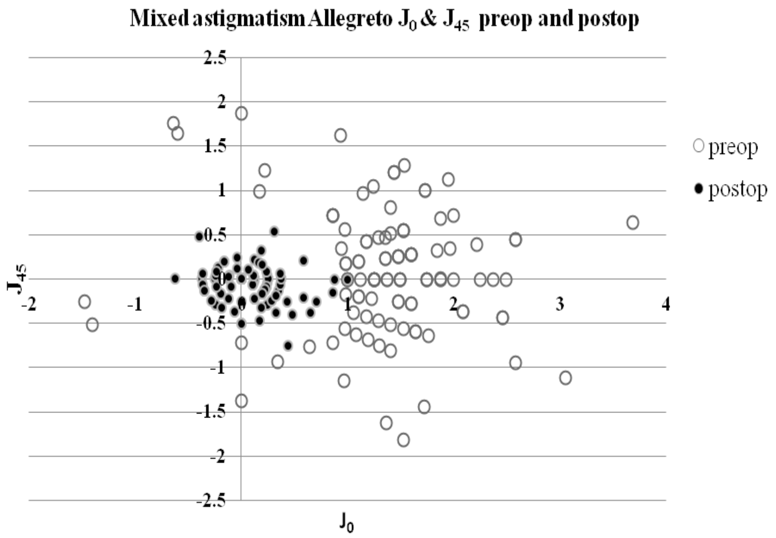
Comparison of the difference (Δ) between the pre- and postoperative J_{45} vector values with preoperative J_{45} values. The least squares regression lines equating ΔJ_{45} and preoperative J_{45} were as follows:

Group 3, ΔJ_{45} = 0.926 J_{45} + 0.045 (r=0.934, n=61, p<0.001).

Group 4, ΔJ_{45} = 1.020 J_{45} + 0.032 (r=0.974, n=111, p<0.001).

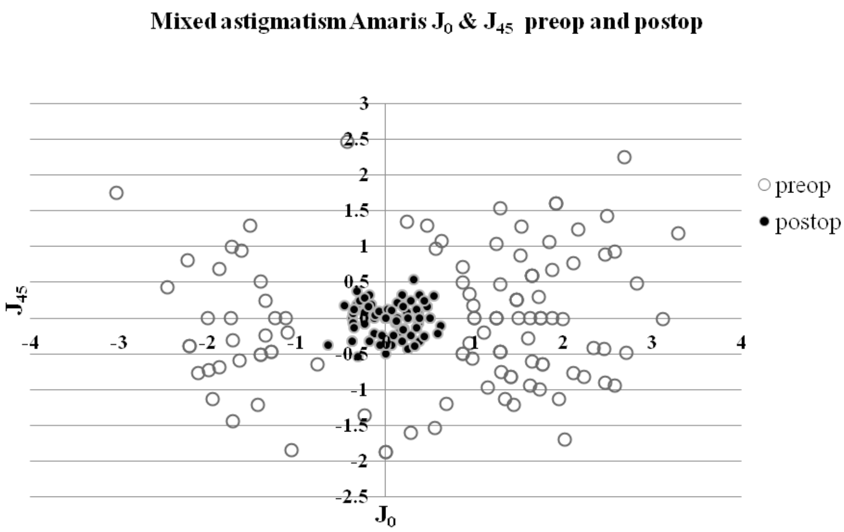
The difference between these two correlation coefficients was significant (z=−2.886, p=0.004).

FIGURE 22. Association between pre- and postoperative values of J_0 and J_{45} for group 3 – Mixed astigmatism corrected with Wavelight Allegretto Eye-Q platform.



In the group 3, preoperative r=0.238 (p=0.065) and postoperative r=−0.028 (p=0.833). Treatments are working to nullify astigmatism (vector values are converging towards zero) but they don't achieve it completely.

FIGURE 23. Association between pre- and postoperative values of J_0 and J_{45} for group 4 – Mixed astigmatism corrected with Amaris 750 S platform

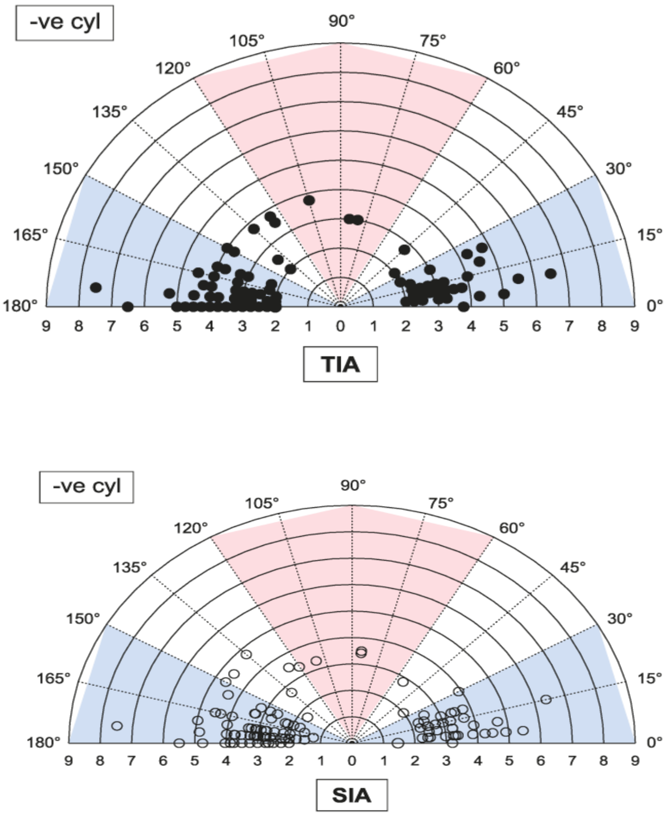


In the group 4, preoperative r=0.104 (p=0.277) and postoperative r=0.030 (p=0.754). Vector values are converging towards zero, but they are not zero. Treatments are working very good, but not excellent, because still some residual astigmatism is still present postoperatively.

5.3.2. ALPINS METHOD

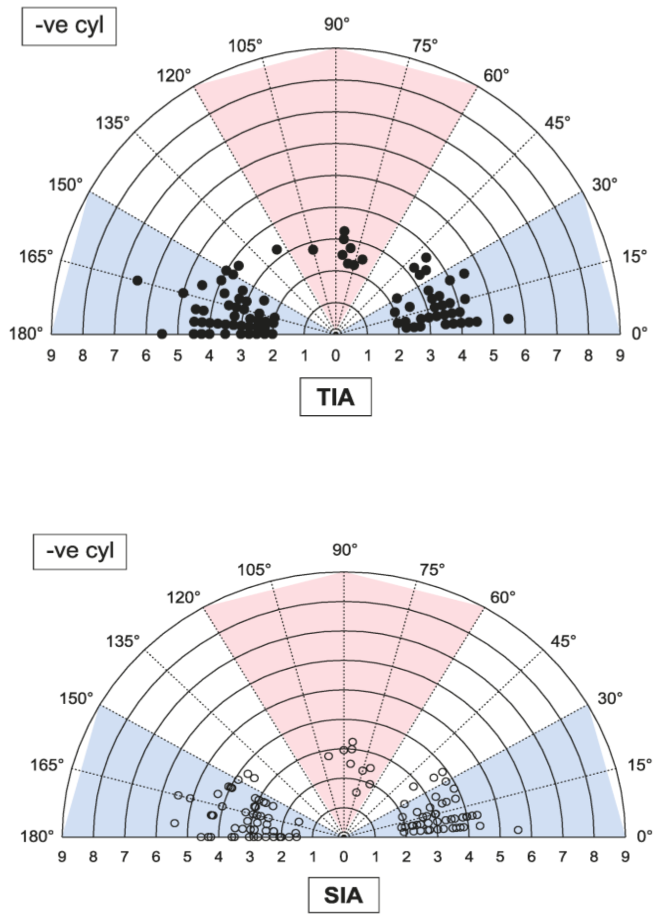
5.3.2.1. MYOPIC ASTIGMATISM

FIGURE 24. Comparison of target induced astigmatism and surgically induced astigmatism for group 1 – Myopic astigmatism corrected with Allegretto Eye-Q platform



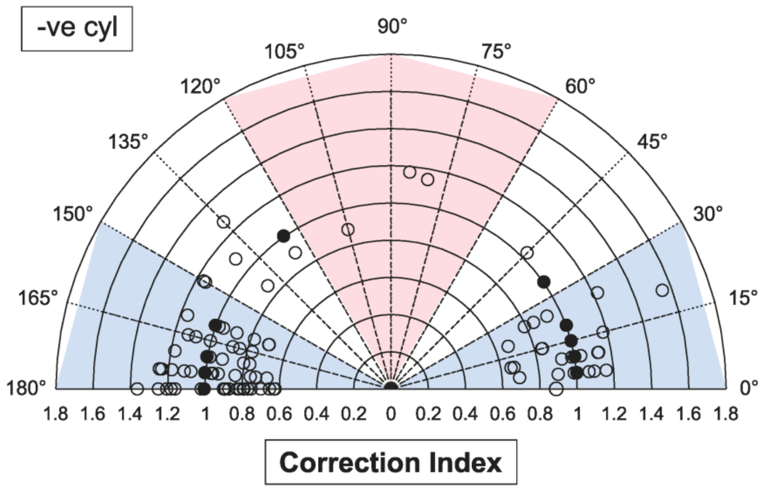
These are polar diagrams where TIA (filled circles) and SIA (unfilled circles) data are compared. The values along x-axis are negative. There are more unfilled circles inside the 2.00 D semicircle than filled circles. This points toward undercorrection of astigmatism.

FIGURE 25. Comparison of target induced astigmatism and surgically induced astigmatism for group 2 – Myopic astigmatism corrected with Amaris 750S platform



In these polar diagrams TIA (filled circles) and SIA (unfilled circles) data are compared, and the values along x-axis are negative. Inside the 2.00 D there are more unfilled than filled circles that indicates undercorrection of astigmatism.

FIGURE 26. Ratio of surgically induced /target induced astigmatic power and the intended axis of astigmatic correction for group 1 – Myopic astigmatism corrected with Allegretto platform (group 1)



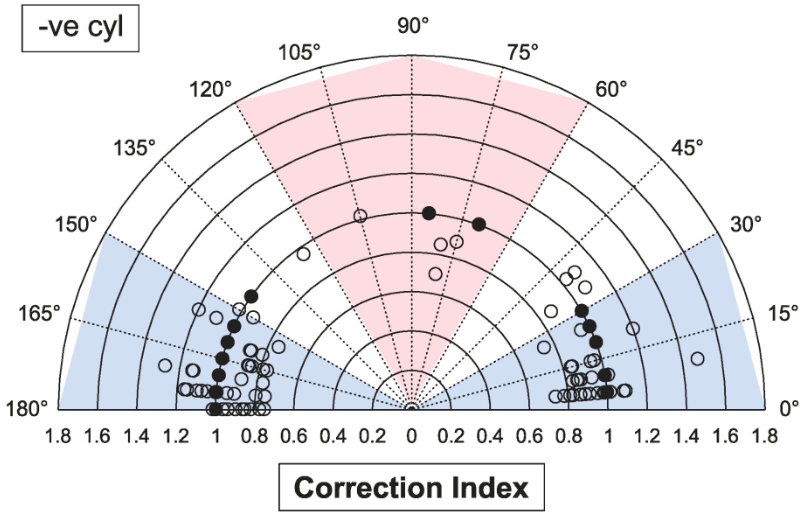
This polar diagram is showing the ratio of the TIA and SIA in relation to the intended axis of astigmatic correction. The horizontal x-axis represents the ratio ranging from 0 to up to 1.8 from the center outward in 0.2 steps. The loci of the most data points occur between the 0.6 and 1.2 ratios. The filled circles are the loci where the ratios equal one. Ideally, all data points should lie on the '1.0' semicircle.

Multiple linear regression analysis revealed significant association between the SIA power (y_1), sine of the axis (y_2), TIA power (x_1), and sine of the axis (x_2). The equations are following:

y_1=0.829x_1-0.403x_2-0.325 (r =0.804, p<0.001, r_{power} = 0.799, p_{power} = <0.001, r_{axis} = 0.074, p_{axis}=0.466)

y_2=0.951x_2-0.007x_1+0.008 (r =0.950, p<0.001, r_{power} = 0.008, p_{power} = 939, r_{axis} = 0.950, p_{axis}<0.001)

FIGURE 27. Ratio of surgically induced / target induced astigmatic power and the intended axis of astigmatic correction for group 2 – Myopic astigmatism corrected with Amaris 750S platform



The ratio of the TIA and SIA in relation to the intended axis of astigmatic correction is showed on this polar diagram. The loci of the most data points take place between the 0.6 and 1.2 ratios on horizontal x-axis, where the ratio is ranging from 0 to up to 1.8 from the center outward in 0.2 steps. The filled circles are the loci where the ratios equal one. Ideally, all data points should be located on the '1.0' semicircle.

Multiple linear regression analysis revealed significant association between the SIA power (y_1), sine of the axis (y_2), TIA power (x_1), and sine of the axis (x_2). The equations are following:

y_1=0.891x_1-0.039x_2-0.192 (r=0.897, p<0.001, r_{power} = 0.897, p_{power} = <0.001, r_{axis} = 0.060, p_{axis}=0.521)

y_2=0.856x_2-0.007x_1+0.105 (r=0.832, p<0.001, r_{power} = 0.092, p_{power} = 0.329, r_{axis} = 0.074, p_{axis}<0.001)

FIGURE 28. Comparison of surgically induced and target induced astigmatic powers for group 1 – Myopic astigmatism corrected with Allegretto Eye-Q platform

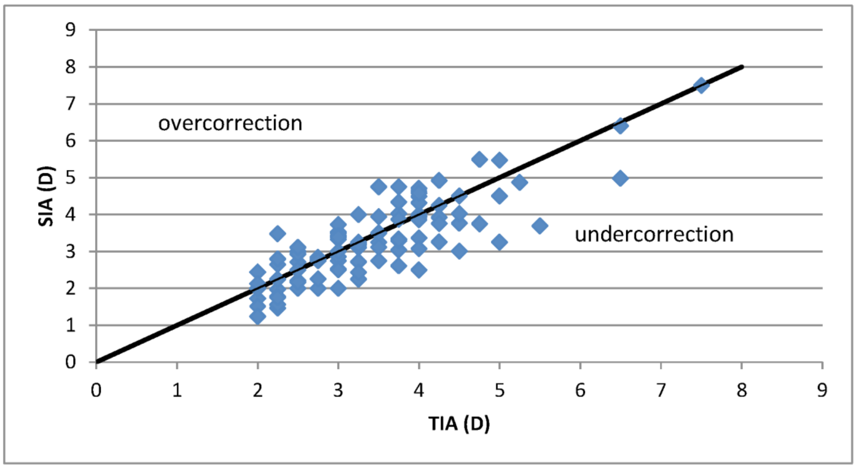
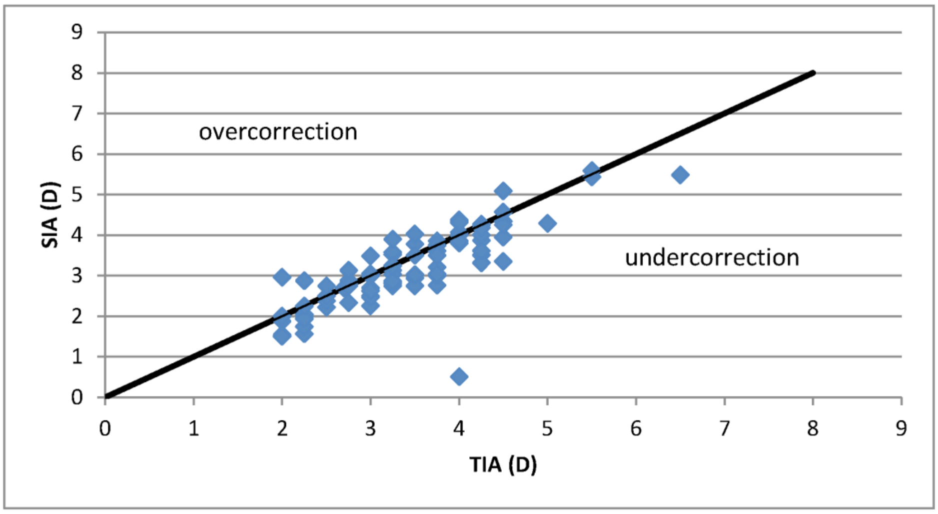


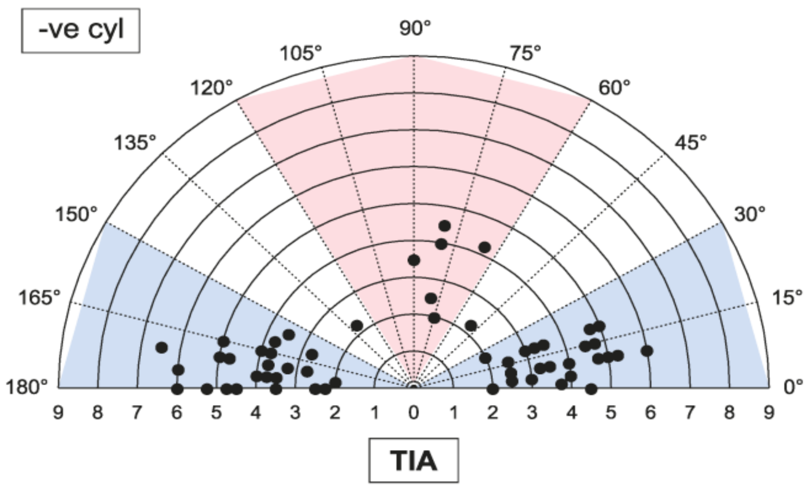
FIGURE 29. Comparison of surgically induced and target induced astigmatic powers for group 2 – Myopic astigmatism corrected with Amaris 750S platform



Figures 28 and 29 compare the TIA and SIA powers. The solid line represents the surgically induced = target induced astigmatic power. Most data points are below the one-to-one line which points toward undercorrection of astigmatism.

5.3.2.2. MIXED ASTIGMATISM

FIGURE 30. Comparison of surgically induced astigmatism and target induced astigmatism for group 3 – Mixed astigmatism corrected with Allegretto Eye-Q platform



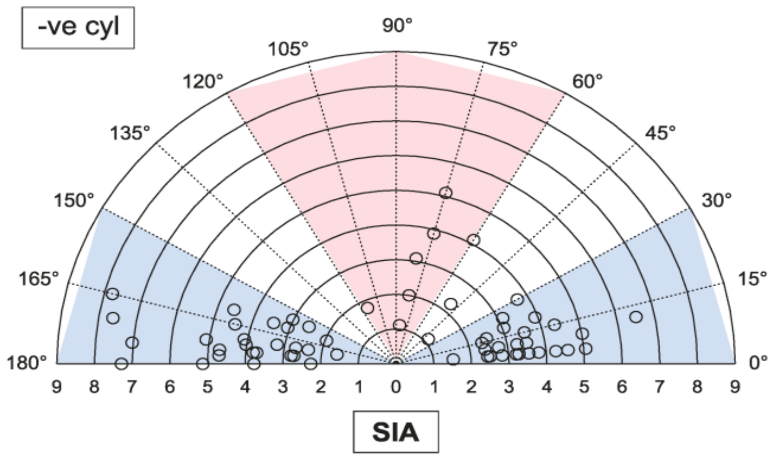
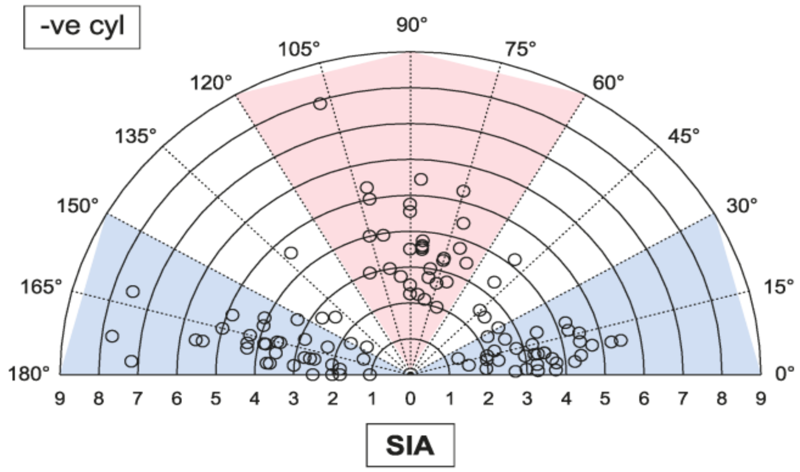
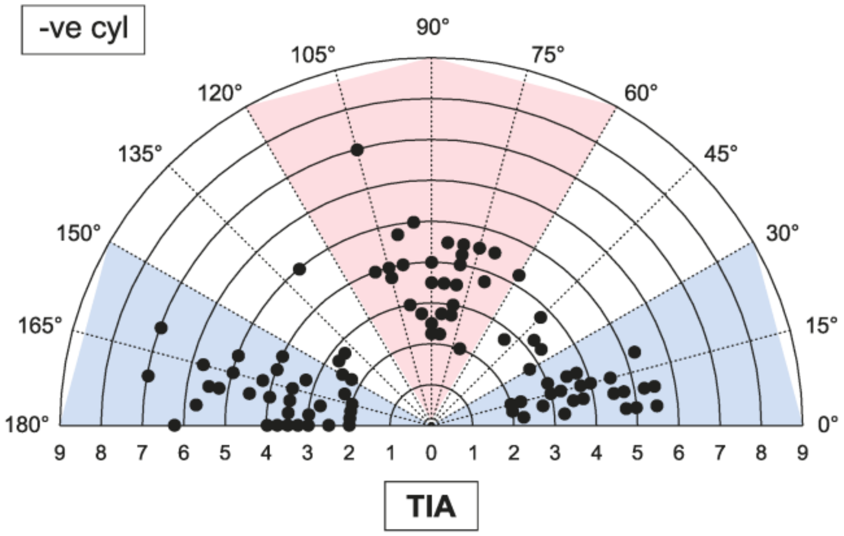


FIGURE 31. Comparison of surgically induced astigmatism and target induced astigmatism for group 4 – Mixed astigmatism corrected with Amaris 750S platform

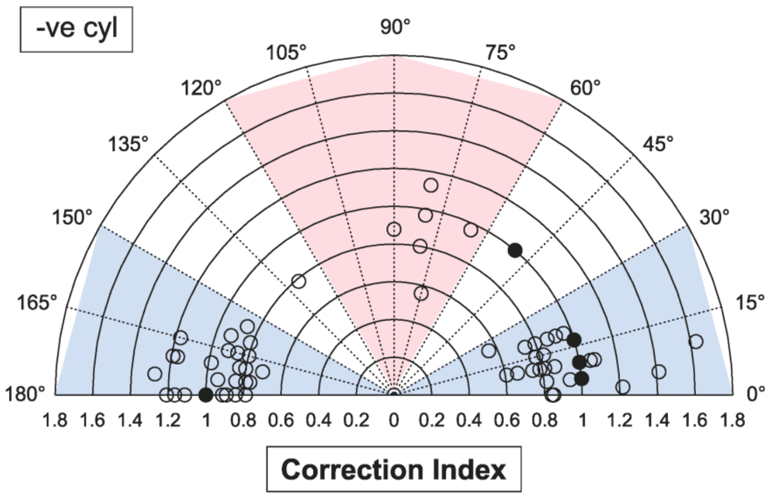




Surgically induced astigmatism (SIA) and target induced astigmatism (TIA) are defined in 4.2.7.2. in Methods section.

Figures 30 and 31 are polar diagrams where SIA (unfilled circles) and TIA (filled circles) data are compared, and the values along x-axis are negative. Because there are more unfilled circles inside the 2.00 D semicircle than filled circles it points toward undercorrection of astigmatism.

FIGURE 32. Ratio of surgically induced /target induced astigmatic power and the intended axis of group 3 – Mixed astigmatism corrected with Allegretto Eye-Q platform



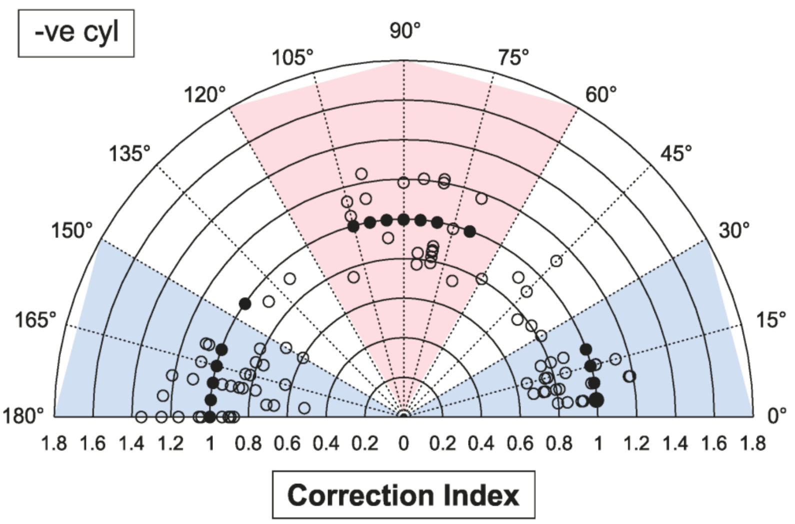
Polar diagram is showing the ratio of the SIA and TIA in relation to the intended axis of astigmatic correction. The horizontal x-axis represents the ratio ranging from 0 to up to 1.8 from the center outward in 0.2 steps. The loci of the most data points occur between the 0.6 and 1.2 ratios. The filled circles are the loci where the ratios equal one. Ideally, all data points should lie on the '1.0' semicircle.

Multiple linear regression analysis revealed significant association between the SIA power (y_1), sine of the axis (y_2), TIA power (x_1), and sine of the axis (x_2). The equations are following:

y_1=1.063x_1-0.233x_2-0.411 (r=0.881, p<0.001, r_{power} = 0.880, p_{power} <0.001, r_{axis} = 0.239, p_{axis} = 0.076)

y_2=0.953x_2-0.009x_1+0.075 (r=0.963, p<0.001, r_{power} = 0.256, p_{power} =0.053, r_{axis} = 0.962, p_{axis}<0.001)

FIGURE 33. Ratio of surgically induced /target induced astigmatic power and the intended axis of group 4 – Mixed astigmatism corrected with Amaris 750S platform



Polar diagram has the same characteristics as in the previous figure (Figure 32) showing the ratio of the SIA and TIA in relation to the intended axis of astigmatic correction.

Multiple linear regression analysis revealed significant association between the SIA power (y_1), sine of the axis (y_2), TIA power (x_1), and sine of the axis (x_2). The equations are following:

y_1=1.029x_1-0.115x_2-0.322 (r=0.908, p<0.001, r_{power} = 0.907, p_{power} <0.001, r_{axis} = -0.013, p_{axis}= 0.811)

y_2=0.977x_2-0.004x_1+0.002 (r=0.990, p<0.001, r_{power} = -0.010, p_{power} = 0.91, r_{axis} = 0.990, p_{axis}<0.001)

FIGURE 34. Comparison of surgically induced and target induced astigmatic powers for group 3 – Mixed astigmatism corrected with Allegretto Eye-Q platform

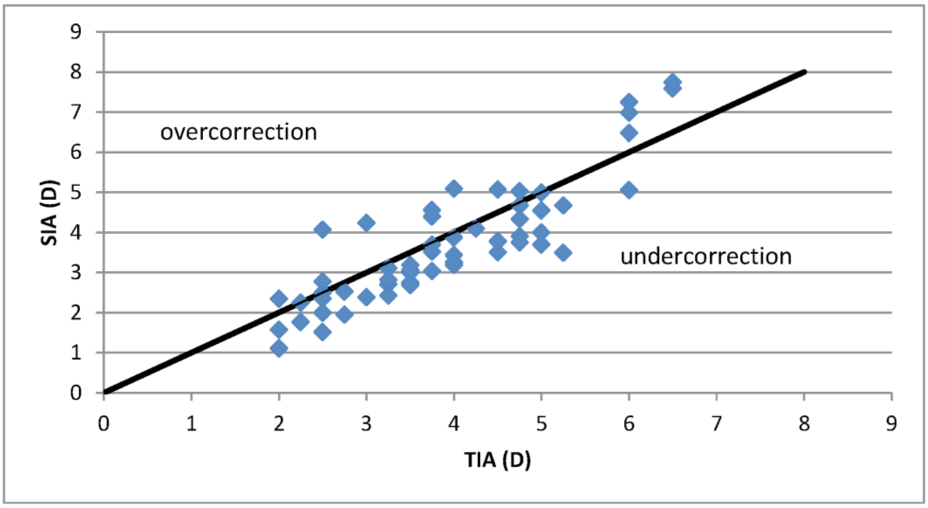
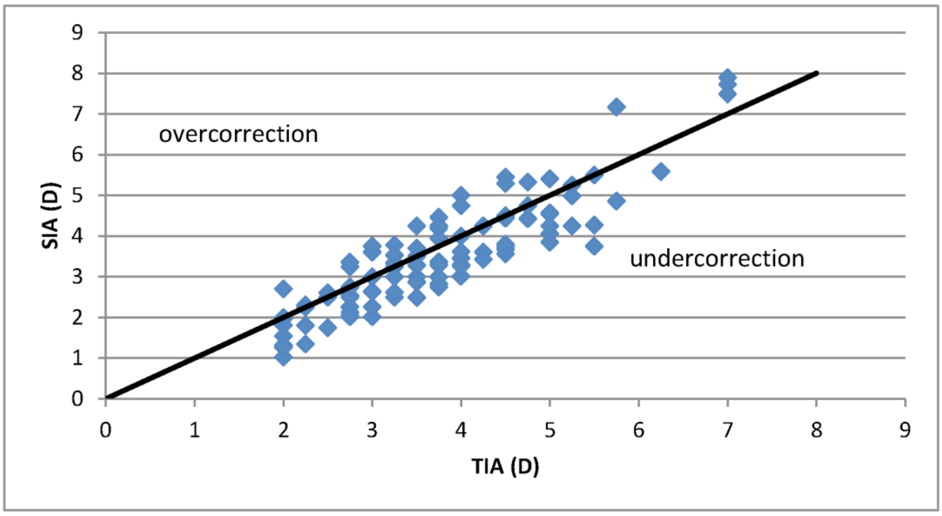


FIGURE 35. Comparison of surgically induced and target induced astigmatic powers for group 4 – Mixed astigmatism corrected with Amaris 750S platform



Figures 34 and 35 compare the SIA and TIA powers of mixed astigmatism groups. The solid line represents the surgically induced = target induced astigmatic power. Most data points are below the solid line which points toward undercorrection of astigmatism.

FIGURE 36. Average Angle of Error (Δθ) for each of the four groups

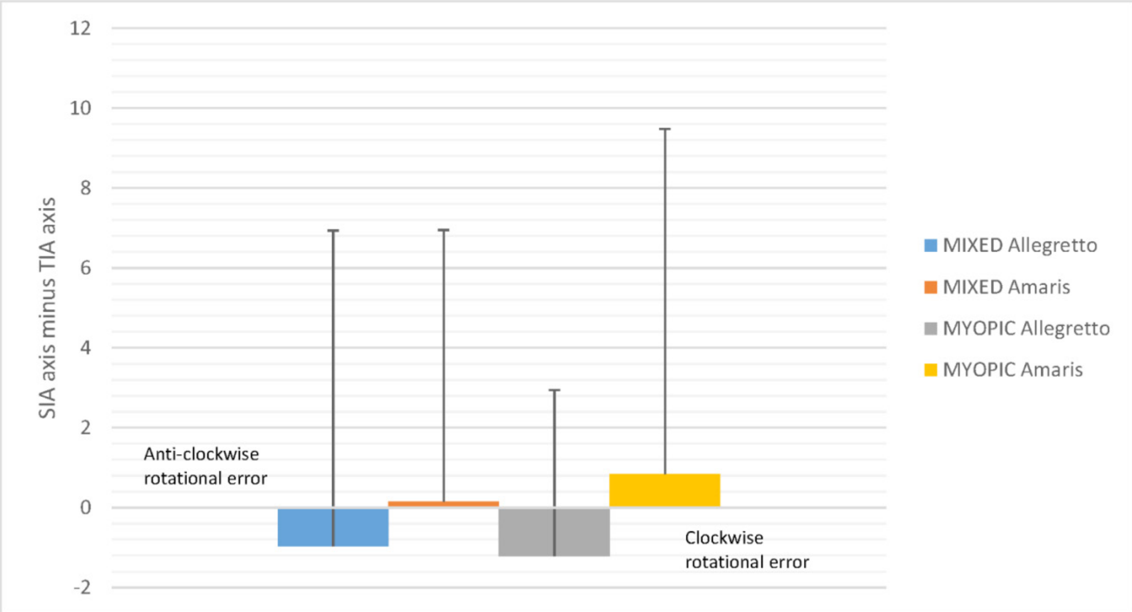


Figure 36 is a histogram showing the average angle of error (angle between the surgically induced astigmatism and target induced astigmatism – SIA minus TIA axis). The y-axis is the difference in degrees where a negative value indicates a clockwise rotational error and a positive value indicates the opposite. The 'T' bars are the upper positive standard deviation values.

The mean±standard deviation (SD) values for Δθ (difference between the SIA axis minus TIA axis) were -1.22°±4.17° for group 1 – Myopic astigmatism treated with Wavelight Allegretto Eye-Q, +0.80°±8.64° for group 2 – Myopic astigmatism treated with Schwind Amaris 750S, -0.96°±7.90° for group 3 – Mixed astigmatism treated with Wavelight Allegretto Eye-Q, and+0.15°±6.79° for group 4 – Mixed astigmatism treated with Schwind Amaris 750S.

Only the difference between group 1 – Myopic astigmatism treated with Wavelight Allegretto Eye-Q and group 2 – Myopic astigmatism treated with the Schwind Amaris 750S was revealed to be significant (p=0.020).

TABLE 14.

SIA Power and Axes Predicted Using the Multilinear Regression Equations								
Group a	*F*	*R*	*P*	N	r power	*p* power	r axis	*p* axis
Group 1 (myopic astigmatism corrected with Allegretto Eye-Q)								
$y_1=0.829x_1-0.403x_2-0.325$	87.76	0.804	<0.001	127	0.799	<0.001	0.074	0.466
$y_2=0.951x_2-0.007x_1+0.008$	446.58	0.950	<0.001	127	0.008	0.939	0.950	<.001
Group 2 (myopic astigmatism corrected with Amaris 750S)								
$y_1=0.891x_1-0.039x_2-0.192$	230.39	0.897	<.001	119	0.897	<0.001	0.060	0.521
$y_2=0.856x_2+0.007x_1+0.105$	277.35	0.832	<.001	119	0.092	0.329	0.912	<.001
Group 3 (mixed astigmatism corrected with Allegretto Eye-Q)								
$y_1=1.063x_{1+}0.233x_{2+}0.411$	990.09	0.881	<.001	61	0.880	<0.001	0.239	0.076
$y_2=0.953x_2+0.009x_1+0.075$	362.60	0.963	<.001	61	0.256	0.053	0.962	<.001
Group 4 (mixed astigmatism corrected with Amaris 750S)								
$y_1=1.029x_{1-}0.115x_2+0.322$	270.12	0.908	<.001	111	0.907	<.001	-0.013	0.811
$y_2=0.977x_2+0.004x_1+0.002$	2.910.90	0.990	<.001	111	-0.010	0.91	0.990	<.001

SIA=surgically induced astigmatism

5.4. HIGH ORDER ABERRATIONS RESULTS

There was no statistically significant difference (p>0.05) in preoperative higher order aberrations coma, trefoil and spherical aberration (SA) between the group 1 – myopic astigmatism corrected with Wavelight Allegretto Eye-Q and group 2 – myopic astigmatism corrected with Schwind Amaris 750S platform.

5.4.1. MYOPIC ASTIGMATISM

TABLE 15. High order aberrations on 5mm pupil of group 1 – Myopic astigmatism corrected with Allegretto Eye-Q platform

High-order aberrations — myopic astigmatism			
Wavelight Allegretto Eye-Q			
Variable	*Mean±standard deviation*		
	Preop	*Postop*	*p value**
coma (μm)	0.12±0.09 (0.01 to 0.53)	0.11±0.10 (0.01 to 0.90)	0.592
trefoil (μm)	0.11±0.06 (0.01 to 0.32)	0.11±0.13 (0.01 to 0.90)	0.999
SA (μm)	−0.02±0.07 (−0.28 to 0.20)	0.00±0.05 (−0.40 to 0.22)	0.056

There was no significant change between preoperative and postoperative high-order aberrations. Although there was no difference in SA between preoperative and postoperative values, SA showed a tendency to shift towards more positive values in 54.4% of eyes, and in 42.4% of eyes showed a tendency to shift towards negative values, while 3.2% of eyes remained unchanged.

TABLE 16. High order aberrations on 5mm pupil of group 2 – Myopic astigmatism corrected with Amaris 750S platform

High-order aberrations — myopic astigmatism			
Schwind Amaris 750S			
Variable	*Mean±standard deviation*		
	Preop	*Postop*	*p value**
coma (μm)	0.11±0.08 (0.00 to 0.40	0.13±0.11 (0.01 to 0.80)	0.166
trefoil (μm)	0.10±0.06 (0.01 to 0.29)	0.09±0.08 (0.01 to 0.49)	0.211
SA (μm)	−0.01±0.05 (−0.23 to 0.10)	−0.01±0.07 (−0.26 to 0.14)	0.504

There was no significant change between preoperative and postoperative high-order aberrations. There was no difference in SA between preoperative and postoperative values, but SA shifted towards more positive values in 41.5% of eyes, in 50.0% towards negative values, and in 8.5% of eyes remained unchanged.

5.4.2. MIXED ASTIGMATISM

TABLE 17. High order aberrations on 5mm pupil of group 3 – Mixed astigmatism corrected with Allegretto Eye-Q platform

High-order aberrations — mixed astigmatism			
Wavelight Allegretto Eye-Q			
Variable	Mean±standard deviation		
	Preop	*Postop*	*p value**
coma (μm)	0.12±0.08 (0.02 to 0.45)	0.10±0.06 (0.04 to 0.28)	0.347
trefoil (μm)	0.13±0.13 (0.01 to 0.90)	0.10±0.05 (0.02 to 0.26)	0.116
SA (μm)	0.02±0.06 (−0.11 to 0.14)	0.00±0.04(−0.09 to 0.12)	0.03

There was no significant change in coma and trefoil, while spherical aberration shifted from positive to negative values. SA showed a tendency to shift towards negative values in 63.3% of eyes, and in 26.7% of eyes showed a tendency to shift towards more positive values, while 10.0% of eyes remained unchanged.

TABLE 18. High order aberrations on 5mm pupil of group 4 – Mixed astigmatism corrected with Amaris 750S platform

High-order aberrations — mixed astigmatism			
Schwind Amaris 750S			
Variable	*Mean±standard deviation*		
	Preop	*Postop*	*p value**
coma (μm)	0.12±0.09 (0.01 to 0.46)	0.11±0.03 (0.01 to 0.53)	0.420
trefoil (μm)	0.10±0.07 (0.01 to 0.44)	0.09±0.08 (0.01 to 0.76)	0.404
SA (μm)	0.02±0.05 (−0.07 to 0.20)	0.00±0.04 (−0.18 to 0.10)	<0.001

Spherical aberration shifted from positive to negative values while there was no significant change in coma and trefoil. SA showed a tendency to shift towards negative values in 66.1% of eyes, in 29.4% of eyes showed a tendency to shift towards more positive values, in 4.5% of eyes remained unchanged.

There was no significant difference in the magnitude of high-order aberrations between the lasers for mixed astigmatism (coma p=0.222, trefoil p=0.314, SA p=1.00).

6. DISCUSSION

Laser in situ keratomileusis (LASIK) is regarded as the most performed elective procedure in medicine. It is estimated that almost 1,000,000 people per year have a LASIK procedure in the USA. [189, 190]

Causes of LASIK popularity are based on various factors – no postoperative pain, fast recovery of visual acuity, refractive predictability and acuracy, and minimal incidence of intraoperative and postoperative complications. [191, 192-195]

LASIK is a highly successful surgical treatment for correcting myopia and low levels of hyperopia. However, treatment of astigmatism, especially hyperopic astigmatism, is still a therapeutic challenge and often results in significant refractive misscorrections. [196, 197]

Correcting astigmatism accurately with any refractive procedures is still a challenge. Refractive surprises following LASIK for astigmatism may stem from a variety of sources such as, an error in the preoperative refraction, keying in the wrong correction into the laser delivery program, misorientation of the ablating beam relative to the exact axis of astigmatism, lack of adequate consistency in the energy distribution within the photoablating beam, unexpected shifts in corneal bulk distribution during the postoperative healing period affecting the topography of corneal optical interfaces, errors in postoperative refraction. Sources of error may be self-limiting, some maybe accumulative and others may cancel each other out.

Patients with high astigmatism pose a particular challenge in refractive laser surgery because the treatment has a lower predictability and, possibly, stability. Laser ablation of high astigmatism is technically more demanding due to the alignment of the elliptic ablation axis and the compensation for cyclorotation and coupling effect of the sphere component. [198-202]

Recent advances in excimer laser technology, such as the use of aspheric ablation profiles, incorporation of higher-order aberration treatment, and eye trackers, have presumably led to better refractive outcomes and reduced induction of higher-order aberrations postoperatively. [203]

6.1. VISUAL ACUITY

Overcorrection, undercorrection, and residual or induced astigmatism are commonly noted after LASIK. [202, 203]

Although unpredictable wound healing and corneal biomechanical changes [204] are thought to underlie corrections that deviate from the preoperative plan in most cases, the specific aetiology is not clear.

Uncorrected distance visual acuity (UDVA) is one of the most important parameters in estimating the success of a LASIK procedure. UDVA is directly linked with residual refractive error, and it is especially important when it comes to evaluation of astigmatic excimer laser ablations, when the residual astigmatism is actually expected in some patients. Loss of lines of corrected visual acuity are not uncommon. This can be associated with the biomechanical response of the cornea following treatment coupled with the exact properties of the astigmatic ablation profile and the effective optical zone of the cornea that was photoablated.

For group 1 – myopic astigmatism corrected with Allegretto values of postoperative UDVA showed improvement in comparison to preoperative CDVA, the difference was 0.5 Snellen lines and was statistically significant (p=0.017).

For group 2 – myopic astigmatism corrected with Amaris 750S improvement in postoperative UDVA in comparison to preoperative CDVA was 0.5 Snellen line and was not statistically significant (p=0.06).

For group 3 – mixed astigmatism corrected with Allegretto, the values of postoperative UDVA showed improvement in comparison to preoperative CDVA, the difference was 0.3 Snellen lines and was not statistically significant (p=0.406).

For group 4 – mixed astigmatism corrected with Amaris 750S – improvement in postoperative UDVA in comparison to preoperative CDVA was observed but improvement of 0.3 Snellen lines was not statistically singnificant (p=0.115)

None of the eyes lost any lines of CDVA.

Chayet reported [106] no loss of corrected visual acuity when treating myopic and mixed astigmatism using the Nidek EC-5000 excimer laser (Nidek Company, Gamagori, Japan). Out of 86 eyes, no eye lost more than 1 line of corrected visual acuity, and 22 eyes (25%) gained 1 or more lines of corrected visual acuity.

Rueda reported [205] a loss of two lines of corrected visual acuity in treatment of mixed and simple myopic astigmatism with Nidek EC-5000 excimer laser. Out of 65 eyes ten percent (four eyes) lost two lines of Snellen CDVA, whereas 35% (14 eyes) gained one or more lines.

Moshirfar's study [206] showed loss of one line of CDVA for group of patients with myopic and mixed astigmatism treated on WaveLight Allegretto Wave Eye-Q 400 Hz laser platform, which was caused by a persistent irregular astigmatism confirmed by topography, in absence of a flap complications.

6.1.1. MYOPIC ASTIGMATISM

All patients had significant improvement of uncorrected visual acuity in comparison to the preoperative values. This was expected and innkeeping with decrease of refractive error. Values of postoperative UDVA were even better than the preoperative CDVA. This result should be interpreted with caution regarding the fact that preoperatively patients were tested with trial lenses. The aberrations and magnifications associated with trial lenses can, in themselves, impact on CDVA. When it comes to the high compound astigmatism, glasses cause degradation of image quality, and therefore it leads to decrease of corrected visual acuity. It may be better to compare preoperative corrected visual acuity with postoperative uncorrected visual acuity even if the patients were preoperatively tested with their contact lenses.

Both platforms showed high and acceptable levels of safety because there was no loss of lines of corrected visual acuity in any of the tested groups.

The results found in this study are similar to Ziaei et al. [207] who report high levels of safety with Wavelight Allegretto Eye-Q excimer laser platform. This report noted no loss of acuity lines after treating 887 eyes with low to moderate myopic astigmatism using the WaveLight Allegretto Eye-Q excimer laser platform.

Arbealez et al. [161] used LASIK for the surgical correction of low to moderate myopia with astigmatism using the Schwind Amaris excimer laser and reported that at six months postoperatively uncorrected visual acuity was 20/20 or better in 98% (351 of 358 treated eyes) and no eyes lost two or more lines of corrected distant visual acuity.

Tomita et al. [208] used LASIK to correct myopia or myopic astigmatism using the Amaris 750 S excimer laser. They reported that no eye lost any lines of CDVA. All eyes had a postoperative CDVA of 20/20 or better.

Stonecipher and Kezirian [159] reported no loss of lines of corrected visual acuity of patients with myopic astigmatism treated on WaveLight Allegretto Wave excimer laser with either wave-front-optimized or wavefront-guided treatment, three months postop. None of the eyes that received these treatments lost two lines or more of corrected distant visual acuity (CDVA).

6.1.2. MIXED ASTIGMATISM

All patients had significant improvement of uncorrected visual acuity in comparison to preoperative values, which is in direct correlation with decreasement of refractive error. Values of postoperative UDVA were comparable with preoperative CDVA. Both platforms showed high level safety because there was no loss of lines of CDVA in either of the groups. Our results are similar to Kilavuzoğlu group of patients treated on Technolas 217z100 excimer laser.

Kilavuzoğlu et al. [209] compared the results of WaveLight Allegretto Eye-Q 400 Hz and Technolas 217z 100 excimer lasers in the treatment of mixed astigmatism. Twenty-eight eyes of 21 patients were treated with WaveLight and 46 eyes of 28 patients were treated with the Technolas excimer laser. Three months postoperatively, 70% of patients treated with WaveLight and 100% of patients treated with Technolas had an uncorrected distance visual acuity of 20/25 or better (p=0.211).

There was an improvement in UDVA and no loss in CDVA for both lasers. In group 4 postoperative UDVA was better than preoperative CDVA.

Stonecipher and Kezarian [159] found no loss of CDVA at 6 months using the Allegretto 400 Hz platform. Stonecipher reports that at six months,10% of 137 eyes with mixed astigmatism treated with the Wavelight Allegretto 200 Hz excimer laser platform lost one line of corrected distance visual acuity (CDVA) whereas no eyes treated with the 400 Hz system lost any lines of CDVA.

Alió et al. [210] using the Amaris 500 platform with an aspheric profile reported 16% of cases lost up to one line of CDVA.

Lui et al. [211] reported safety of Nidek EC-5000 excimer laser in 66 astigmatic eyes with cylinder from 4.00 to 8.00 D (myopic, hyperopic and mixed astigmatism) where no eyes lost any lines of corrected visual acuity.

Alió et al. [212] reported that Laser in situ keratomileusis was performed on 40 eyes using the Visx 20/20 excimer laser. At 15 years follow-up the postoperative CDVA was significantly better than preoperative CDVA (p<0.001).

Kilavuzoğlu et al. [209] found that at 3 months, none of the eyes lost any lines of CDVA and 2 eyes gained ≥2 lines of CDVA in the WaveLight group (28.5%). In the Technolas group at month 3, none of the eyes lost any lines of CDVA and 2 eyes gained ≥1 line(s) of CDVA (20%).

Pinelli et al. [213] reported that there was no loss of lines of CDVA and 16 (40%) eyes gained 1 line in CDVA at postoperative 1 year with the Technolas 217 excimer laser.

De Ortueta and Haecker [214] reported that no single eye lost more than one line of corrected visual acuity for patients that underwent LASIK treatment of mixed astigmatism using the Schwind Esiris Laser platform. Out of 19 eyes no eye lost more than one line of CDVA, while a gain of two lines was found in 5% at three months, and 6% at six and twelve months postop.

6.2. REFRACTIVE RESULTS

Residual refractive errors are the most common cause of patient unsatisfaction. [215]

Despite technological improvements, residual postoperative refractive errors are still an issue that need to be dealt with, especially when they interfere with the patient´s quality of life.

Patients with myopia and myopic astigmatism were included in this study. Maximum amount of sphere correction was up to -8.50 D, and up to – 7.50 D of cylindrical correction. Preoperatively there was no statistically significant difference between the groups. Postoperatively significant reduction of refractive errors was, as expected, encountered.

6.2.1. MYOPIC ASTIGMATISM

In both groups (1 and 2) there was almost complete elimination of spherical refractive error. In group 1 (myopic astigmatism corrected with Allegretto-Eye Q platform) postoperative amount of spherical refractive error was −0.16 DS (s.d, ±0.46, range −1.50 DS to 1.00 DS, p<0.001); and in group 2 was −0.16 DS (s.d, ±0.55, range −2.00 DS to 1.25 DS, p<0.001). There was no statistically significant difference between the groups which leads up to the conclusion that both groups were equally successful in eliminating spherical refractive errors. Nowadays, the majority of commercially available excimer laser platforms are good or excellent in correcting of spherical refractive errors, because the algorithms for spherical correction are much simpler in comparison to astigmatic profiles.

Both groups had significant reduction in astigmatism, but it was not completely eliminated. Postoperative values of astigmatism in group 1 were −0.55 DC (s.d, ±0.46 range −2.25 DC to 0.00, p<0.001); and in group 2 were −0.43 DC (s.d, ±0.36 range−1.50 DC to 0.00, p<0.001, and there was no statistically significant difference between the groups either pre- or postoperatively.

Correction of the sphere was very acceptable for both lasers; however, there was a tendency towards residual cylinder. When analysing eyes with myopic astigmatism, 48% of cases were within ±0.50 D of intended refraction in the first (Allegretto group), in comparison to 54% in the third (Amaris) group (p =0.368). Our results differ from those of Stonecipher et al. [159] who reported 94% out of 186 cases treated with Wavelight Allegretto 400 Hz within ±0.50 D of intended correction.

Alió et al. [210] used the Amaris 500 platform with an aspheric profile, and reported a predictability of 87%. However, those data were based on 37 eyes, whereas our study was based on 119 eyes using a different Amaris platform. The differences between studies may result from different patient selection criteria rather than different platforms.

Teus et al. [216] did an observational, cross-sectional study of 116 consecutive myopic eyes with −3.00 D or more of astigmatism that underwent LASIK surgery The mean residual reractive cylinder 3 months postoperatively was −0.78±0.83 D (range, −3.00 to 0.00 D).

6.2.2. MIXED ASTIGMATISM

In both groups (3 and 4) almost complete elimination of spherical refractive error was registered. In group 3 (Mixed astigmatism corrected with Wavelight Allegretto Eye-Q platform) postoperative amount (fraction) was 0.77 DS (s.d, ±0.20 range+0.20 to +1.00, $p<0.001$) and in group 4 (Mixed astigmatism corrected with Amaris 750S excimer laser platform) was 0.80 DS (s.d, ±0.21 range +0.05 to +1.00, $p<0.001$). There was no statistically significant difference between the groups either pre- or postoperatively which leads us to conclusion that both groups were equally successful in eliminating spherical refractive error.

Both groups had significant reduction in astigmatism, but it was not completely eliminated. Postoperative values of astigmatism in group 3 were −0.85 DC (s.d, ±0.41 range −2.00 DC to 0.00), $p<0.001$); and in group 4 were −0.58 DC (s.d, ±0.38 range−1.50 DC to 0.00, $p<0.001$, and there was not statistically significant difference between the groups.

Mean values of residual cylinder do not adequately describe the astigmatic corrections as noted in 4.2.7 section. Cylinders cannot be measured and described with just one number because astigmatism has both magnitude and direction. The magnitude can give us some perspective regarding success and potential patient satisfaction considering that residual refractive errors are the most common cause of patient unsatisfaction.

When analysing eyes with mixed astigmatism, 28% of cases were within ±0.50 D of intended refraction in the group 3, in comparison to 42% of eyes in the group 2 ($p=0.060$). Our results to some extent correlate to the study by Alió et al. [210] which reported significant undercorrection of mixed astigmatism using Amaris 500 and Aberration-Free profile. Alió reported 26.9% of patients being within ±0.50 D of the attempted correction, and 65.3% being within ±1.0 D.

Stonecipher et al. [158] reported the opposite outcome on Allegretto 400 Hz, with 100% of patients having ≤0.50 D of residual astigmatism with r2 values >0.98.

Kilavuzoğlu et al. [209] used WaveLight Allegretto Wave Eye-Q 400 Hz and Technolas 217z 100 excimer lasers in the treatment of mixed astigmatism in 49 patients. With Wavelight cylindrical refractive errors at month 3 were –0.92 D (s.d, ± 0.28 D) and –0.88 D (s.d, ± 0.46 D), with Technolas 217z 100. At month 3 in the WaveLight vs. the Technolas group, spherical equivalent values were -0.38 ± 0.73 D and -0.33 ± 0.20 D, respectively. They only had 49 patients so their results are quite limited compared to results in this investigation because of number of patients included in the study.

6.3. VECTOR ANALYSES OF REFRACTIVE RESULTS

Predicting a change in spherical refractive error is relatively simple involving just two numbers and a subtraction. However, predicting the outcome of treating astigmatism is more complex because astigmatism involves two figures: power and axis. Thus, astigmatism can be treated as a vector because it has a magnitude and directional quality as covered in 4.2.7 of this thesis.

6.3.1. Thibos method

6.3.1.1. Myopic astigmatism

There was no significant difference of mean J_0 values between the two groups before surgery. Therefore, for statistical purposes, the two sets of cases can be considered as being drawn from the same population.

After treatment, the two groups still remained mutually indistinguishable, but clearly the surgical treatment reduced the value of J_0 vector, showing that both platforms reduced astigmatism as expected. The percentage change in the J_0 vector was 93% and 95% for the Allegretto and Amaris platforms respectively. Using the Nidek 500 platform, Abolhassani et al. [217] reported a 103% shift in J_0 vector. Such a change can only occur if the sign of the J_0 vector changed from plus to minus or vice versa. In our cases, the mean J_0 vector fell in value but still remained positive. Turning to the J_{45} vector, there was no significant difference between the two groups preop and postop. However, we did detect a slight difference postop at the p=0.012 level, and the variance in the data is responsible for masking the true significance in the difference between the +0.0051 and −0.0581 mean J_{45} values. According to the vector, the two laser platforms are not producing totally identical results.

The J_{45} vector describes the astigmatism in the oblique meridian, in contrast to the J_0 vector, which describes astigmatism in the vertical and horizontal meridian. This suggests that one platform is tending to produce a more precise correction, or offering a better treatment, along the oblique meridian compared with the other. In a perfect scenario, the treatment should reduce the J_0 and J_{45} vectors to near zero. Referring to Table 12, the Amaris platform reduced the J_{45} vector to a mean of 0.0051, and the Allegretto reduced it to −0.0581.

Thus, it appears that for myopic astigmatism the Amaris platform is preferred when the presenting axis of astigmatism is predominantly oblique. In cases when the myopic astigmatic axis is either with or against the rule, there is no detectable difference in performance between the two platforms. Abolhassani et al. [217] reported a 76.4% fall in the average value for the J_{45} vector. We found J_{45} vector to change by 176% and 102% for the Allegretto and Amaris platforms respectively. Table 12 shows the signs of the mean values shifted from plus to minus for the Allegretto cases, but the opposite was found in the Amaris cases. This indicates that besides reducing astigmatism, the two platforms are not producing identical endpoint results as noted earlier.

6.3.1.2. Mixed astigmatism

The two groups were mutually distinguishable before treatment. After treatment, the two groups were mutually indistinguishable, but clearly the treatment reduced the value of the J_0 vector, showing that the two platforms reduced astigmatism as expected. On a percentage basis, the changes in both vectors are similar to those reported by Abolhassani et al. [217]

Postop, the J_{45} vector showed that there was no difference between the two groups before and after treatment.

Furthermore, it appears neither of the platforms significantly reduced the values of J_{45} vectors. This suggests that treatment had no real effect on J_{45} vectors. This may be a statistical anomaly, because the J_0 vector certainly did reduce very significantly.

This unforeseen result may be due to the fact that in most cases the astigmatism was predominantly either with or against the rule. Very few cases presented with oblique astigmatism.

The question remains as to why the J_0 vector was different between the two groups preop but not postop. Referring to the formulae used to calculate J_0 and J_{45}, the preop J_0 values between the two groups could differ either because the cylinder power in one group was higher than the other or because the mean and range of axes in one group was weighted differently.

By process of elimination, the two groups differed because in one group the axis of astigmatism was predominantly with the rule, and against the rule in the other one.

Nevertheless, postoperatively the two populations converged to become mutually indistinguishable.

The correlations between changes in vector compared with preoperative values and J_0 and J_{45} before and after treatment.

Glancing at Figs. 16, 17, 20 and 21, the strong correlations between changes in the vector values with preop values were expected.

In both myopic and mixed astigmatism, the slope values for the cases treated using the Allegretto platform are less than one. The nomogram for the Allegretto procedure advises the surgeon to intentionally undercorrect the astigmatism by 25%. Based on our previous experience, we adjusted the nomogram, undercorrecting by 15%. Therefore, encountering a slope value <1.00 was to be expected. However, the slope values revealed using the Amaris platform were ≥1.00, and the corresponding correlation coefficients were consistently higher compared with the Allegretto cases. The significant differences between the platforms lead us to conclude that the outcome of the Amaris procedure can be predicted with more reliability compared with the Allegretto procedure. The refractive surgeon is more likely to reach the desired endpoint refraction using the Amaris procedure when attempting to correct moderate to high myopic or mixed astigmatism.

Glancing at Figs. 18, 19, 22 and 23, we would expect the vector values to converge towards the 0.0 point after the treatment. A lack of convergence towards the 0.0 coordinate would be counter-intuitive, suggesting that the treatment was of no clinical value. The postop data show the vector values collapsing towards a cluster about the 0.0 point. The cluster, as opposed to a single point, demonstrates that the treatments are working to nullify astigmatism but not completely cancel it out. In other words, some residual astigmatism is still present after sophisticated surgery. Even to this day, a small but significant amount of residual astigmatism is not unexpected. [216]

The area covered by the Amaris-treated cases is lower than the area covered by the Allegretto-treated cases, indicating that the former is more accurate than the latter.

There was no significant correlation when we compared J_0 with J_{45} either preop or postop for each of the two platforms. This is not surprising when we consider that the majority of cases presented in this study were either with or against the rule astigmatism. In such cases, the J_0 vector by definition will always have a much greater value compared with J_{45}. For example, when the preop astigmatism is −3.00 dcyl×180, J_0 is 1.500 and J_{45} is −0.004. For the Allegretto-treated cases, the correlation between J_0 and J_{45} for mixed astigmatism group preop was 0.238 and for a two-tailed test the p value was 0.063 reducing to 0.032 for a single-tailed test. To avoid making an erroneous conclusion, we accept the result of the two-tailed test. This correlation reduced to −0.028 postop. The difference between these two correlation coefficients appears to be significant, but a posthoc analysis proved otherwise (Fisher's r to z transformation z=1.47, p=0.142).

6.3.2. Alpins method

Methods to calculate differences between, and changes of, astigmatic powers and axes have previously developed. [218-224]

The individual algorithms and equations may appear different from each other, but the computed results are almost the same. The data points in Figures 24, 25, 30 and 31 do not show any obvious pattern or trend between the SIA and TIA powers and axes. This implies that any difference between SIA and TIA is random or obscured by other factors. However, closer inspection of Figures 24, 25, 30 and 31 shows there are more unfilled circles inside the 2.00 D semicircle than filled circles. This clearly points toward undercorrection of astigmatism in all four groups. Turning to Figures 26, 27, 32 and 33, there is a clear tendency toward undercorrection because the SIA/TIA ratios are mainly concentrated in the semicircles between 0.4 and 1.0. Some of the figures show that the ratio is greater than unity along a particular axis of correction, but the figures do not reveal an obvious association between the ratio and the target axis.

The expressions resulting from both multiple and single linear regression analysis show a significant undercorrection of myopic astigmatism. Figures 28, 29, 34 and 35 show the tendency toward an undercorrection in all four groups. To some extent, the appearance of the data in Figures 28, 29, 34 and 35 and results of linear regression come as no surprise, considering more than 70% of cases presented with astigmatism of 0.50 D or greater at 1 year postoperatively. A difference between a pair of SIA and TIA powers values could be due to the typical error in subjective refraction, which is reported to range from ±0.34 D in the younger population and ±0.51 D in the older population. [225-227]

The high significance of the multiple and single linear regression analyses would not have encountered if differences between SIA and TIA arose from totally random events associated with subjective refraction alone.

Our aim was to ascertain whether systematic rotational misorientation and/or miscorrection could be responsible for differences between SIA and TIA. Figure 25 shows that the mean difference between the SIA and TIA axes ($\Delta\theta$) was negative for cases treated with the WaveLight Allegretto platform and positive for cases treated with the Schwind Amaris platform. This shows there was a tendency toward a clockwise angle of error greater than 1° when the WaveLight Allegretto platform was used to correct myopic astigmatism and an anticlockwise angle of error of less than 1° for the Schwind Amaris platform. Other studies have reported a tendency toward undercorrection of astigmatism in cases treated by LASIK.[177, 210, 228-230]

These reports rarely commented on the angle of error between the SIA and TIA axes; thus, we cannot directly compare our findings with others. Figures 26, 27, 32 and 33 also feature large error bars, which clearly point toward wide variations between cases. Nevertheless, linear regression resulted in and indicating that the difference between the SIA and TIA in terms of both power and axis is directly related to the TIA for myopic astigmatism treated using the Schwind Amaris platform. For TIA axes of 45° and 90°, predicts SIA axes of 44° and 70°, respectively (i.e., a rise in the $\Delta\theta$ value from 1° to 20°). Clearly, the difference between SIA and TIA axes is predicted to increase as the TIA axis shifts toward the vertical, according to the cases included in this study.

Table 18 shows the SIA power and axes values predicted using the multiple linear regression equations for TIA corrections of −3.00 and −6.00 DC with axes ranging from 0° to 135°. The predictions demonstrate the validity and practical value of these regression analyses. For both platforms, there is a tendency toward under-correction and angles of error less than 5° when treating either oblique or with-the-rule astigmatism. When the TIA has an oblique axis of 45° or 135°, an angle of error of 1° is predicted when the correction is −3.00 DC, rising to 3° for a correction of −6.00 DC. However, according to the results of our analyses, this angle is predicted to be more profound when the astigmatism is against-the-rule. In the case of myopic astigmatism, the Schwind Amaris platform is predicted to under-correct −6.00 DC by less than 0.50 D, but the angle of error ($\Delta\theta$) is predicted to rise from 4° when the astigmatism is with-the-rule to 22° when the astigmatism is against-the-rule (TIA axis of 90°). This is 2° greater compared with the prediction for the Schwind Amaris platform according to, pointing to the likely influence of TIA power on Δθ. Using the WaveLight Allegretto platform, Table 18 shows Δθ is predicted to rise from 1° to 14° when comparing a correction for mixed astigmatism of −6.00 × 180 with −6.00 x 90. The predictions regarding against-the-rule astigmatism have to be viewed with caution because, as Figures 26, 27, 32 and 33 show, only a minority of our cases were treated for a negative cylinder where the axis was 90° ± 15°. At this point, proposing a hypothesis to account for the differences in the predicted angles of error between with-the-rule and against-the-rule astigmatic corrections predicted by the multi-linear regression analyses would be speculative. On the other hand, it would not be unreasonable to suggest that over time the accumulated effects of the ocular adnexa on the ocular surface coupled with the dynamics of healing are less favorable toward against-the-rule astigmatism.

TABLE 19. Examples of SIA Power and Axes Predicted Using the Multilinear Regression Equations for Each Group.

Examples of SIA Power and Axes Predicted Using the Multilinear Regression Equations for Each Group				
		Axis		
Platform	**0º**	**45º**	**90º**	**135º**
-3.00 DC				
Group 1	-2.81DCx178	-3.10DCx45	-3.21DCx79	-3.10DCx135
Group 2	-2.87DCx5	-2.89DCx44	-2.90DCx70	-2.89DCx134
Group 3	-2.73DCx177	-2.56DCx46	-2.50DCx87	-2.57DCx136
Group 4	-2.54DCx1	-2.62DCx45	-2.66DCx83	-2.62DCx135
-6.00 DC				
Group 1	-5.30DCx177	-5.59DCx47	-5.70DCx91	-5.59DCx137
Group 2	-5.54DCx4	-5.57DCx42	-5.58DCx68	-5.57DCx132
Group 3	-5.99DCx179	-5.83DCx44	-5.77DCx76	-5.83DCx134
Group 4	-5.63DCx1	-5.71DCx46	-5.74DCx95	-5.71DCx136
SIA = surgically induced astigmatism; DC=diopters cylinder				

The WaveLight Allegretto and Schwind Amaris platforms feature sophisticated built-in mechanisms to ensure any astigmatic correction remains on target and along the inputted axis. The Allegretto platform has a high-speed camera operating at 400 Hz to track the patient's eye movements and compensates for shifts in eye position or interrupts the treatment if the eye moves outside a preset range during treatment. The Schwind Amaris platform has a five-dimensional 1050 Hz infrared eye tracker with continuous limbus, pupil, iris recognition, and cyclotorsion tracking integrated into the laser delivery process. Irrespective of these high levels of sophistication and precision, our results show that axis rotational errors are evident at 1 year postoperatively. Each individual result is the culmination of the unique characteristics of the laser used, the energy distribution over the region of ablation, and the effects of healing of the treated cornea. Nevertheless, on average the WaveLight Allegretto platform has a tendency toward a systematic clockwise axis rotational error, whereas the Schwind Amaris platform tends toward the opposite.

The company that manufactures the WaveLight Allegretto platform advises surgeons to use the Wellington nomogram before photoablation. This nomogram advises the surgeon to reduce the astigmatic correction by 25%. In our series, we elected to reduce the correction by 15%.

Table 19 shows that for both platforms the SIA power has a propensity to be lower than the TIA and this was most profound when the WaveLight Allegretto platform was used to correct relatively high myopic astigmatism.

Morlet et al. [231] noted that interpreting the results of astigmatic vector analysis can be awkward. In the analysis, the attempt to obviate from distorting the reality of refractive outcomes was critical. The processes used revealed that both platforms were similar in tending to undercorrect astigmatism; axis rotational errors were apparent, although overall the two platforms differed in terms of direction; and the predicted angle between the SIA and TIA tended to increase when the astigmatic correction was against-the-rule.

The use of a simple single spherical equivalent as an index does not reflect the efficacy and accuracy of compound astigmatism correction. Therefore, separate analyses of refractive outcomes separating sphere, cylinder, and axis would be more reasonable to evaluate surgery for astigmatism. This could also facilitate any nomogram adjustment, with the aim of further enhancing the accuracy of treatment.

Figures 12, 13, 14 and 15 demonstrate that there is a highly significant association between the attempted astigmatic correction, achieved astigmatic correction, and the difference between the attempted and achieved (ΔC) amount of astigmatic correction. With closer scrutiny of our data, we noticed that residual cylinder tended to remain in the same axis direction (sd ±20°) as the preop uncorrected astigmatism. From that observation, it was noticed that both lasers tend to undercorrect the astigmatism. However, in several cases with cylindrical corrections of ≥6.0 D, both lasers overcorrected and sometimes (though it was rare) the postoperative axis shifted by near 90°. Observations such as these could only be made by vector analysis. [232]

6.4. HIGH ORDER ABERRATIONS

There was no significant change in high-order aberrations in eyes with myopic astigmatism. This finding supports the definition underlying the aspheric profiles that were designed to keep high-order aberrations of the eyes unchanged after photoablation. Arbelaez et al. [164] found a statistically significant increase in high-order aberrations after myopic astigmatism treatment on Amaris 500, which was in correlation with the amount of refractive error treated. However, the amount of induced aberrations was lower than that from conventional treatment. [164]

Stonecipher et al. [159] did not find a change in high-order aberration in myopic astigmatism up to 3.0 D using wavefront optimized profile from Allegretto Eye-Q. Our data confirm the earlier findings using the Allegretto profile, but not the findings using the earlier Amaris profile. In eyes with mixed astigmatism, changes in amount of spherical aberration have been reported with a tendency towards more negative values; however, the changes were below clinical significance. [233-235]

We found similar, but statistically significant, trends towards negative values for both lasers, and this support the findings of Alió et al. [210] using the Amaris 500.

In summary, both lasers produced acceptable results tending to preserve optical performances of the eye without significant induction of high-order aberrations. There is no difference in effectiveness between lasers for spherical correction.

However, Schwind Amaris 750S demonstrated better results and less residual cylinder than Wavelight Allegretto Eye-Q. Nevertheless, the correction of both lasers may yield small residual cylinder. Future studies, with more intensive mathematical analysis of astigmatism itself, are needed to further improve formulas and laser nomograms for cylinder correction.

7. CONCLUSIONS

This clinical investigation and analysis led to the following:

1. In this study, LASIK showed comparable safety, efficacy, and predictability for laser correction of high astigmatism (greater than 2 D) in myopic eyes. Predictability of the correction of the cylindrical component was lower than that for the SE. Both lasers produced acceptable results tending to preserve optical performances of the eye without significant induction of high-order aberrations. There is no difference in effectiveness between lasers for spherical correction. However, Schwind Amaris 750S demonstrated better results and less residual cylinder than Wavelight Allegretto Eye-Q. Nevertheless, the correction of both lasers may yield small residual cylinder.

2. In myopic and mixed astigmatism, for both groups, there was a statistically significant improvement in postoperative UDVA and CDVA in comparison to preoperative results. Values of postoperative UDVA tended to show an improvement in comparison to preoperative CDVA. However, the difference was only statistically significant in Allegretto group for my-opic astigmatism. There was no difference in postoperative UDVA or CDVA between lasers for both myopic and mixed astigmatism ($p>0.05$). None of the eyes lost any lines of CDVA.

3. In myopic and mixed astigmatism for both Allegretto and Amaris group there was a statistically significant shift towards zero (i.e. emmetropia) in both postoperative sphere and cylinder in comparison to preoperative values. There was no difference in effectiveness of spherical correction between laser platforms (myopic astigmatism $p=0.969$; mixed astigmatism $p=0.236$). There was a significant difference in effectiveness of cylinder correction between the groups (myopic astigmatism $p=0.027$; mixed astigmatism $p<0.001$). For the Allegretto cases, there was a tendency toward residual cylinder when comparing the attempted cylindrical correction with the postoperative cylinder (myopic astigmatism r=0.3978, $p<0.01$, n=127; mixed astigmatism r=0.4567, $p<0.01$,n =61). The Amaris group had less residual astigmatism than the Allegretto group, and the difference was significant (myopic astigmatism $p=0.027$; mixed astigmatism $p<0.001$).

4. There was a highly significant association between the attempted and achieved astigmatic corrections for both platforms (myopic astigmatism Allegretto $R^2=0.7874$ and Amaris $R^2=0.8335$; mixed astigmatism Allegretto $R^2=0.8894$ and Amaris $R^2=0.8805$).

5. In myopic astigmatism there was a statistically significant difference between J_0 preop and J_0 postop for both platforms ($p<0.001$). There was no statistically significant difference for J_0 postoperatively between the platforms ($p=0.380$). There was no statistically significant difference between J_{45} preop and J_{45} postop for either platform ($p=0.042$ and 0.685 for the Allegretto and Amaris groups respectively. There was a statistically significant difference for J_{45} postoperatively

between the platforms (*p*=0.012). The difference (Δ)between the pre- and postop J_0 vector values with pre-op J_0 values was significant for both platforms (*p*<0.001) and between the platforms (z=−3.086, *p*=0.002).

6. Both platforms significantly reduced astigmatism. In an ideal situation the postoperative J_0 and J_{45} values should be zero. They were not. The smallest value was 0.005 for the myopic astigmatic cases treated with Amaris in relation to the J_{45} vector. The highest value was 0.1085 for the mixed astigmatism cases treated with Allegretto in relation to the J_0 vector. Other methods of vector analysis of astigmatism [245, 250] may yield different results, but for this study the techniques we used were relatively simple, producing viable results. Emsley [238] said that Franciscus Cornelius Donders (1818–1889) was the first to introduce cylindrical lenses for measurement and correction of astigmatism. To this day, we do not have a universally accepted system for assessing change in ocular astigmatic power and axis. The procedure advocated by Thibos et al. [190] can be considered as a simple and robust tool for this purpose.

7. By using Alpins method, in our analysis we have attempted to obviate from distorting the reality of refractive outcomes. The processes we used revealed that both platforms were similar in tending to undercorrect astigmatism; axis rotational errors were apparent, although overall the two platforms differed in terms of direction; and the predicted angle between the SIA and TIA tended to increase when the astigmatic correction was against-the-rule.

8. There was no significant difference in the magnitude of high-order aberrations between the lasers for both the myopic astigmatism (coma *p*=0.137, trefoil *p*=0.143, SA *p*=0.2) and mixed astigmatism groups (coma *p*=0.222, trefoil *p*=0.314, SA *p*=1.00).

9. In myopic and mixed astigmatism, for both groups, there was a statistically significant improvement in postoperative UDVA and CDVA in comparison to preoperative results. Values of postoperative UDVA tended to show an improvement in comparison to preoperative CDVA. However, the difference was only statistically significant in Allegretto group for myopic astigmatism. There was no difference in postoperative UDVA or CDVA between lasers for both myopic and mixed astigmatism (*p*>0.05). None of the eyes lost any lines of CDVA.

7.1. SCIENTIFIC CONTRIBUTION

This prospective trial and the analytical tools used to gain a better understanding of the surgical outcomes, helps us to decipher, interpret and appreciate the differences in the practical performances of two quite dissimilar laser delivery platforms aimed to correct astigmatism. Simple clinical measures of astigmatism subjected to by vector analysis using the techniques proposed by Alpins and Thibos, may prove useful in improving patient counseling. In turn, this could increase clinical success, and patients' overall satisfaction, in the surgical challenge that is astigmatic laser in situ keratomileusis.

8. SUMMARY

Title: Prospective comparison of two excimer laser platforms in treatment of high astigmatism with laser in situ keratomileusis

Author: Alma Biščević

Zagreb, 2018

PURPOSE: Comparison of Wavelight Allegretto Eye-Q and Schwind Amaris 750S excimer laser groups after performed LASIK procedure regarding functional parameters – uncorrected (UDVA) and corrected distant visual acuity (CDVA), residual refractive error, astigmatism outcomes by means of vector analysis and high order aberrations in patients with high astigmatism (more than 2 diopters (D)).

METHODS: 135 patients with myopic astigmatism (246 eyes) and 102 patients with mixed astigmatism (172 eyes) underwent LASIK correction (some of the patients had only one eye operated – the eye that met the criteria for the study, while the other eye had no diopter at all) and were divided in 4 groups: 1 – myopic astigmatism corrected with Allegretto, 2 – myopic astigmatism corrected with Amaris, 3 – mixed astigmatism corrected with Allegretto and 4 – mixed astigmatism corrected with Amaris. Data were analysed to determine significance of change in spherical correction, astigmatism, UDVA, CDVA, high order aberrations, and also vector analysis by Thibos (J_0 and J_{45}) and Alpins method was performed.

RESULTS: Visual acuity improvement for group 1 was statistically significant (p=0.017); for group 2, 3 and 4 was not statistically significant (p=0.06, p=0.406, p=0.115). None of the eyes lost any lines of CDVA. Regarding refractive results, for all groups there was almost complete elimination of spherical and cylindrical refractive error. High-order aberrations results for groups 1 and 2 showed no significant change between preoperative and postoperative high-order aberrations, while in groups 3 and 4 spherical aberrations changed. Vector analysis by Thibos showed statistically significant difference between J_0 preop and J_0 postop for both platforms (p<0.001). There was statistically significant difference for J_{45} postoperatively between the platforms (p=0.012). Correlation between ΔJ_0 and preop J_0 values (groups 1 and 2) showed that the difference between these two correlation coefficients was significant (z=−3.086, p=0.002). There was statistically significant difference in preoperative mean values for J_0 (p<0.001) between the groups 3 and 4. There was a statistically significant difference between J_0 preop and J_0 postop for both platforms (p<0.001). Correlation between ΔJ_0 and preop J_0, and between ΔJ_{45} and preop J_{45} for groups 3 and 4 showed that difference between these two correlation coefficients was significant (z=−3.533, p=0.0004; z=−2.886, p=0.004). Vector analysis by Alpins showed that negative SIA power (y1) was significantly correlated with negative TIA power (x1) and sine of the TIA axis (x2) as follows: [a] i, y1=0.829X1–0.403X2–0.325 (F=87.76,

R=0.804, *P*<0.001, N=127); ii, y1=0.891X1–0.037X2-0.192 (F=240.06, R=0.901, *P*<0.001, N=119) and [b] i, y1=1.063X1+0.233X2+0.411 (F=990.99, R=0.881, *P*<0.001, N=61); ii, y1=1.029X1–0.115X2+0.322 (F=270.12, R=0.908, *P*<0.001, N=111). The sine of negative SIA axis (y2) was significantly correlated with negative TIA power (x1) and TIA axis (x2) as follows: [A] I, y2=0.951x2–0.007x1+0.008 (F=446.58, r=0.950, *p*<0.001, n=127); II, y2=0.856x2+0.007x 1+0.105 (F=277.18, r=0.912, *p*<0.001, n=119) and [B] I, y2=0.953x2 +0.009x1+0.075 (F=362.6, r=0.963, *p*<0.001, n=61); II, y2=0.977x2–0.004x1+0.002 (F=2910.9, r=0.990, *p*<0.001, n=111).

CONCLUSIONS: Both lasers showed effective in terms of UDVA, CDVA, spherical correction, and preservation of high-order aberrations. However, Amaris was more effective in cylinder correction. There was no genuine difference post-operatively between groups treated on two different laser platforms according to the vector analyses by Thibos. By using Alpins method, we revealed that both platforms were similar in tending to undercorrect astigmatism; axis rotational errors were apparent, although overall the two platforms differed in terms of direction; and the predicted angle between the SIA and TIA tended to increase when the astigmatic correction was against-the-rule.

9. SAŽETAK

Prospektivna usporedba dvije laserske platforme u tretiranju visokog astigmatizma laser in situ keratomijeluzom

Autor: Alma Biščević

Zagreb, 2018.

CILJ: Usporedba Wavelight Allegretto Eye-Q 400 Hz i Schwind Amaris 750S excimer laser grupa nakon obavljene LASIK procedure analizirajući sljedeće funkcionalne parametre – nekorigirana (UDVA) i korigirana daljinska vidna oštrina (CDVA), ostatna refrakciona greška, rezultati korigiranog astigmatizma uz pomoć vektorske analize te okularne aberacije višeg reda kod pacijenata sa visokim astigmatizmom (više od 2 dioptrije (D)).

METODE: 135 pacijenata s miopskim astigmatizmom (246 očiju) i 102 pacijenta s miješanim astigmatizmom (172 oka) su podvrgnuta korekciji dioptrije LASIK metodom (kod nekih pacijenata operirano je samo jedno oko koje je ispunjavalo kriterije za studiju, dok drugo oko nije imalo dioptriju) te podijeljena u 4 grupe: 1 – miopski astigmatizam korigiran Allegrettom, 2 – miopski astigmatizam korigiran Amarisom, 3 – miješani astigmatizam korigiran Allegrettom i 4 – miješani astigmatizam korigiran Amarisom. Podaci su analizirani da bi se utvrdio značaj promjene sferne korekcije, astigmatizma, nekorigirane (UDVA) i korigirane vidne oštrine na daljinu (CDVA), okularnih aberacija višeg reda, a vektorska analiza Thibosovom (J_0 and J_{45}) i Alpinsovom metodom je također primijenjena.

REZULTATI: Poboljšanje vidne oštrine za grupu 1 je bilo statistički značajno (p=0.017), a za grupe 2, 3 i 4 nije bilo statistički značajne razlike (p=0.06, p=0.406, p=0.115). Niti jedan pacijent (oko) nije izgubio jedan ili više redova korigirane vidne oštrine nakon obavljenog zahvata. Što se tiče refrakcijskih rezultata, sve četiri grupe su imale skoro potpuno otklanjanje sferne i cilindrične refrakcijske pogreške. Rezultati okularnih aberacija višeg reda za grupe 1 i 2 su pokazali statistički neznačajnu promjenu poslijeoperacijskih u odnosu na prijeoperacijske vrijednosti, dok su se u grupama 3 i 4 sferne aberacije promijenile. Vektorska analiza Thibosovom metodom je pokazala statistički značajnu razliku između prijeoperacijskog J_0 i poslijeoperacijskog J_0 za obje platforme (p<0.001). Za vektor J_{45} se pokazala statistički značajna poslijeoperacijska razlika između platformi (p=0.012). Međusobna povezanost između ΔJ_0 i prijeoperacijskih J_0 vrijednosti (grupe 1 i 2) je pokazala da je razlika između ova dva koeficijenta povezanosti bila statistički značajna ($z=-3.086$, p=0.002). Postojala je statistički značajna razlika u prijeoperacijskim srednjim vrijednostima J_0 (p<0.001) između grupa 3 i 4. Pokazala se i statistički značajna razlika između prijeoperacijskog J_0 i poslijeoperacijskog J_0 za obje platforme (p<0.001). Međusobna povezanost između ΔJ_0 i prijeoperacijskog J_0 te ΔJ_{45} i prijeoperacijskog J_{45} za grupe 3 i 4 je dokazala da je razlika između ovih koeficijenata povezanosti bila značajna ($z=-3.533$, p=0.0004; $z=-2.886$,

p=0.004). Vektorska analiza Alpinsovom metodom je pokazala da negativna SIA vrijednost (kirurški izazvani astigmatizam) (y1) je bila značajno povezana sa negativnom TIA vrijednosti (ciljani astigmatizam) (x1) i sinusom TIA osi (x2) na sljedeći način: [A] I, y1=0.829x1–0.403x2–0.325 (F=87.76, r=0.804, *P*<0.001, N=127); II, y1=0.891x1– 0.037x2–0.192 (F=240.06, r=0.901, *P*<0.001, N=119) i [B] I, y1=1.063x1+0.233x2+0.411 (F =990.99, r=0.881, *P*<0.001, *N*=61); II, y1=1.029x1–0.115x2+0.322 (F=270.12, r=0.908, *P*<0.001, N=111). Sinus negativne SIA osi (y2) je bio značajno povezan sa negativnom TIA vrijednosti (x1) i TIA osi (x2) što pokazuje sljedeće: [A] I, y2=0.951x2–0.007x1+0.008 (F =446.58, r=0.950, *P*<0.001, N=127); II, y2 = 0.856x2+0.007x1+0.105 (F=277.18, r=0.912, *p*<0.001, N=119) and [B] I, y2=0.953x2+0.009x1+0.075 (F=362.6, r=0.963, *p*<0.001, n=61); II, y2=0.977x2–0.004x1+0.002 (F =2910.9, r=0.990, *p*<0.001, n=111).

ZAKLJUČAK: Oba lasera su se pokazala učinkovitim po pitanju nekorigirane (UDVA) i korigirane vidne oštrine na daljinu (CDVA), sferne korekcije i očuvanja aberacija višeg reda. Međutim, Amaris se pokazao učinkovitiji u korekciji cilindara. Nije bilo značajne poslijeoperacijske razlike između grupa korigiranih na dvije različite laser platforme po pitanju vektorske analize po Thibosu. Koristeći Alpinsovu metodu otkrili smo da su se obje platforme ponašale slično hipokorigirajući astigmatizam; bile su očite osne rotacijske pogreške, iako su se u cjelini obje platforme razlikovale po pitanju smjera; a predviđeni kut između SIA i TIA bio je sklon povećanju kada je astigmatska korekcija bila “protiv pravila”.

10. LIST OF REFERENCES:

1. Donaldson DD. A new instrument for the measurement of corneal thickness. Arch Ophthalmol. 1966; 76(1):25-31.
2. Mishima S. Corneal thickness. Surv Ophthalmol. 1968; 13:57-96.
3. Rapuano CJ, Fishbaugh JA, Strike DJ. Nine points corneal thickness measurements and keratometry readings in normal corneas using ultrasound pachymetry. Insight 1993; 18:16-22.
4. Nishida T. Basic Science: Cornea, sclera, and ocular adnexa anatomy, biochemistry, physiology, and biomechanics. In: Krachmer JH, Mannis MJ, Holland EJ, eds. Cornea: Fundamentals of Cornea and External Disease. 2nd ed. St Louis: Mosby Co., 2005. p. 3-26.
5. Komai Y, Ushiki T. The three-dimensional organization of collagen fibrils in the human cornea and sclera. Invest Ophthalmol Vis Sci. 1991; 32:2244-58.
6. Giraud JP, Pouliquen Y, Offret G, Payrau P. Statistical morphometric studies in normal human and rabbit corneal stroma. Exp Eye Res. 1975; 21:221-9.
7. Bron AJ, Tripathy RC, Tripathy BJ. Wolff's Anatomy of the Eye and Orbit. 8th ed. London: Chapman & Hall Co., 1997:233-78.
8. Naylor EJ. Astigmatic difference in refractive errors. Br J Ophthalmol. 1968; 52:422–5.
9. Read, SA, Collins, MJ, Carney LG. A review of astigmatism and its possible genesis. Clinical & experimental optometry. 2007; 90(1):5–19.
10. Leo Angart. Clear Vision Naturally, More about astigmatism Blog [Internet]. Melbourne: Leo Angart 2017 Oct- [accessed on 11.11.2017.] Available on: https://cleareyesight.blog-spot.hr/2017/10/more-about-astigmatism.html
11. "Facts About Refractive Errors". National Eye Institute [Internet]. October 2010. Ar-chived from the original on 2 October 2016. Retrieved 29 September 2016. Available on: https://nei.nih.gov/health/errors/errors
12. Hall GW, Campion M, Sorenson CM, Monthofer S. Reduction of corneal astigmatism at cataract surgery. J Cataract Refract Surg. 1991; 17:407-14.
13. Maloney WF, Grindle L, Sanders D, Pearcy D. Astigmatism control for the cataract sur-geon: a comprehensive review of surgically tailored astigmatism reduction (STAR). J Cataract Refract Surg. 1989; 15:45-54.
14. Kronfeld PC. The Temporal Half-Moon. Trans Am Ophthalmol Soc. 1932; 30:431-56.
15. Jackson E. The general significance of visual tests. Can Med Assoc J. 1932; 26:445-8.
16. Linke SJ, Richard G, Katz T. Prevalence and associations of anisometropia with spherical ametropia, cylindrical power, age and sex in refractive surgery candidates. Invest Ophthalmol Vis Sci. 2011; 52:7538-47.
17. Mitchell, DE, Freeman RD, Westheimer G. Effect of orientation on the modulation sensitivity for interference fringes on the retina. J Opt Soc Am. 1967; 57:246-49.
18. Shlaer S. The relation between visual acuity and illumination. J Gen Physiol. 1937; 21:165-88.

19. Flüeler UR, Guyton DL. Does a tilted retina cause astigmatism? The ocular imagery and the retinoscopic reflex resulting from a tilted retina. Surv Ophthalmol. 1995; 40:45-50.

20. Seyed-Farzad M, Tahvildari M, Z-Mehrjardi H. Physiology of astigmatism. In: Goggin M, ed. Astigmatism – Optics, Physiology and Management. Rijeka: InTech Publishing; 2012. p. 3-14.

21. Foster CS, Azar DT, Dohlman CH. Smolin and Thoft's The Cornea: Scientific Foundations and Clinical Practice. Alphen aan den Rijn: Lippincott Williams & Wilkins; Publishing; 2004. p. 173-189.

22. Ljubic A, Trajkovski V, Stankovic B. Strabismus, refractive errors and nystagmus in chil-dren and young adults with Down syndrome. Ophthalmic Genet.2011; 32:204–11.

23. Mahajan VN. Zernike circle polynomials and optical aberrations of systems with circular pupil. Appl Opt. 1994; 33:8121-24.

24. Iskander DR, Collins MJ, Davis B. Optimal modeling of corneal surfaces with Zernike polynomials. IEEE Trans Biomed Eng. 2001; 48(1):87-95.

25. Thibos LN, Applegate RA, Schwiegerling JT, Webb RH, Members V.S.T. Standards for reporting the optical aberrations of eyes. Vis Sci Appl (OSA Trends in Optics & Photonics). 2000; 35:110-30.

26. Liang J, Grimm B, Goelz S, Bille JF. Objective measurement of wave aberrations of the human eye with the use of a Hartmann-Shack wavefront sensor. J Opt Soc Am A Opt Image Sci Vis. 1994; 11(7):1949–57.

27. Mastropasqua L, Toto L, Zuppardi E, et al. Photorefractive keratectomy with aspheric profile of ablation versus conventional photorefractive keratectomy for myopia correction: six-month controlled clinical trial. J Cataract Refract Surg. 2006; 32:109–16.

28. Lombardo M, Lombardo G. Wave aberration of human eyes and new descriptors of image optical quality and visual performance. Journal of cataract and refractive surgery. 2010; 36(2):313–31.

29. Vasudevan B, Fisher B, Case B, Lam P, Wayman J. Progression of lower and higher-order aberrations: a longitudinal study. BMC Ophthalmol. 2015; 15:11. doi:10.1186/1471-2415-15-11.

30. Prieto PM, Vargas-Martín F, Goelz S, Artal P. Analysis of the performance of the Hartmann-Shack sensor in the human eye. J Opt Soc Am A Opt Image Sci Vis. 2000; 17:1388–98. https://doi.org/10.1364/JOSAA.17.001388

31. Moreno-Barriuso E, Merayo Lloves J, Marcos S, Navarro R, Llorente L, Barbero S. Ocular aberrations before and after myopic corneal refractive surgery: LASIK-induced changes measured with laser ray tracing. Invest Ophthalmol Vis Sci 2001; 42(6):1396–1403

32. Marcos S. Aberrations and visual performance following standard laser vision correction. J Refract Surg. 2001; 17(5): S596–601.

33. Santamaría J, Artal P, Bescós J. Determination of the pointspread function of human eyes using a hybrid optical-digital method. J Opt Soc Am A. 1987; 4(6):1109–14.

34. Güell JL, Pujol J, Arjona M, Diaz-Douton F, Artal P. Optical Quality Analysis System: Instrument for objective clinical evaluation of ocular optical quality. J Cataract Refract Surg 2004; 30(7):1598–9.

35. Neil J. Friedman, M.D. Keratometry blog [Internet]. OphthalmologyWeb: Neil J. Friedman; 2009 – Keratometry: Focusing on Astigmatism. 2009 October 12
[accessed 26.06.2016.]. Available on: http://www.ophthalmologyweb.com/Tech-Spotlights/26530-Keratometry-Focusing-on-Astigmatism/

36. Brody J, Waller S, Wagoner M. Corneal Topography: History, Technique, and Clinical Uses. International Ophthalmology Clinics. 1994; 34(3):197-207.

37. Lopes, B, Ramos, I, Dawson, D, et al. Detection of Ectatic Corneal Diseases Based on Pentacam. Z. Med. Phys. 2016; 26(2): 136–42.

38. Hashemi H, Mehravaran S. Day to Day Clinically Relevant Corneal Elevation, Thickness, and Curvature Parameters Using the Orbscan II Scanning Slit Topographer and the Pentacam Scheimpflug Imaging Device. Middle East Afr J Ophthalmol. 2010; 17(1):44-55.

39. Fu J, Wang X, Li S, Wu G, Wang N. Comparative study of anterior segment measure-ment with Pentacam and anterior segment optical coherence tomography. Can J Ophthalmol. 2010; 45(6):627-31. doi: 10.3129/i10-068.

40. Wang Z, Chen J, Yang B. Posterior corneal surface topographic changes after laser in situ keratomileusis are related to residual corneal bed thickness. Ophthalmology. 1999; 106(2):406-10. doi: 10.1016/S0161-6420(99)90083-0.

41. Seitz B, Torres F, Langenbucher A, Behrens A, Suarez E. Posterior corneal curvature changes after myopic laser in situ keratomileusis. Ophthalmology 2001; 108(4):666-72.

42. Maeda N, Klyce SD, Smolek MK, Thompson HW. Automated keratoconus screening with corneal topography analysis. Invest Ophthalmol Vis Sci 1994; 35(6):2749-57.

43. Guyton DL. Prescribing cylinders: the problem of distortion. Surv Ophthalmol. 1977; 22(3):77-88.

44. Keating MP. An easier method to obtain the sphere, cylinder, and axis from an off-axis dioptric power matrix. Am J Optom Physiol Opt. 1980; 57(10):734-7.

45. Morgan PB, Efron N. A decade of contact lens prescribing trends in the United Kingdom (1996-2005). Cont Lens Anterior Eye. 2006; 29(2):59-68.

46. Michaud L, Barriault C, Dionne A, Karwatsky P. Empirical fitting of soft or rigid gas-permeable contact lenses for the correction of moderate to severe refractive astigmatism: a comparative study. Optometry. 2009; 80(7): 375-83. doi: 10.1016/j.optm.2008.11.008.

47. Waring GO III, Lynn MJ, Mc Donnell PJ et al. Results of the Prospective Evaluation of Radial Keratotomy (PERK) Study 10 years after surgery. Arch Ophtalmol. 1994; 112(10):1298-1308.

48. Salamon SA, Hjortdal JO, Ehlers N. Refractive results of radial keratotomy: a ten-year retrospective study. Acta Ophthalmol Scand. 2000; 78(5):566-8.

49. Waring GO III. Radial keratotomy for myopia. South Med J. 1981; 74(1):1-3.

50. Filatov V, Vidaurri-Leal JS, Talamo JH. Selected complications of radial keratotomy, photo-refractive keratectomy, and laser in situ keratomileusis. Int Ophthalmol Clin. 1997; 37:123– 48.

51. Grady FJ. Radial keratotomy for astigmatism. Ann Ophthalmol. 1984; 16(10):942-4.

52. Schiotz LJ. Hin Fall von hochgradigem Hornhautstastigmatismus nach Staarextraction: Bessergung auf operativem Wege. Arch Augenheilkd. 1885; 15:178.

53. Faktorovich EG, Maloney RK, Price FW Jr. Effect of astigmatic keratotomy on spherical equivalent: results of the Astigmatism Reduction Clinical Trial. Am J Ophthalmol. 1999; 127(3):260-9.

54. Nichamin LD. Astigmatism control. Ophthalmol Clin North Am. 2006; 19(4):485-93.

55. Price FW, Grene RB, Marks RG, Gonzales JS. Astigmatism reduction clinical trial: a multicenter prospective evaluation of the predictability of arcuate keratotomy: evaluation of surgical nomogram predictability. Arch Ophthalmol. 1995; 113(3):227-82.

56. Holmes-Higgin DK, Burris TE, Asbell PA, Durrie DS, Schanzlin DJ. Topographic predicted corneal acuity with intrastromal corneal ring segments. J Refract Surg. 1999; 15(3):324-30.

57. Holmes-Higgin DK, Baker PC, Burris TE, Silvestrini TA. Characterization of the aspheric corneal surface with intrastromal corneal ring segments. J Refract Surg 1999; 15(5):520-28.

58. Durrie DS, Asbell PA, Schanzlin DJ. The ICR (intrastromal corneal ring): one-year results of a phase II study in myopic eyes. American Academy of Ophthalmology Final Program. 1995;101.

59. Schanzlin DJ, Abbot RL, Asbell PA et al. Two-year outcomes of intrastromal corneal ring segments for the correction of myopia. Ophthalmology. 2001; 108(9):1688-94.

60. Colin J, Cochener B, Savary G, Malet F, Holmes-Higgin D. INTACS inserts for treating keratoconus: one year results. Ophthalmology 2001; 108(8):1409-14.

61. Siganos CS, Kymionis GD, Kartakis N, Theodorakis MA, Astyrakakis N, Pallikaris IG. Management of keratoconus with Intacs. Am J Ophthalmol 2003; 135(1):64-70.

62. Avni-Zauberman N, Roofman DS: Cross-linking and intracorneal ring segments-review of the literature. Eye Contact Lens. 2014; 40(6):365-70. doi: 10.1097/ ICL.0000000000000091.

63. Vazirani J, Basu S. Keratoconus: current perspectives. Clin Ophthalmol 2013; 7:2019-30. doi: 10.2147/OPTH.S50119.

64. Hofling-Lima AL, Branco BC, Romano AC et al. Corneal infections after implantation of intracorneal ring segments. Cornea. 2004; 23(6):547-9.

65. Coskunseven E, Kymionis GD, Tsiklis NS et al. Complications of intrastromal corneal ring segment implantation using a femtosecond laser for channel creation: a survey of 850 eyes with keratoconus. Acta Ophthalmol 2011; 89(1):54-7. doi: 10.1111/ j.1755-3768.2009.01605.x.

66. Trokel SL, Srinivasan R, Braren B. Excimer laser surgery of cornea. Am J Ophthalmol. 1983; 96(6):710-5.

67. Srinivasan R. Ablation of polymers and biological tissue by ultraviolet lasers. Science. 1986; 234(4776):559–65.

68. Seiler T, Kahle G, Kriegerowski M. Excimer laser (193 nm) myopic keratomileusis in sighted and blind human eyes. Refract Corneal Surg. 1990; 6(3):165-73.

69. Corbett MC, O'Brart DP, Marshall J. Do topical corticosteroids have a role following excimer laser photorefractive keratectomy? J Refract Surg. 1995; 11(5):380-7.

70. Solomon KD, Donnenfeld ED, Raizman M et al. Safety and efficacy of ketorolac tromethamine 0.4% ophtalmic solution in post-photorefractive keratectomy patients. J Cataract Refract Surg. 2004; 30(8): 1653-60.

71. Collins MJ, Carney LG. A review of astigmatism and its possible genesis. Clin Exp Optom. 2007; 90(1):5-19. doi: 10.1111/j.1444-0938.2007.00112.x.

72. Majmudar PA, Forstot SL, Dennis RF et al. Topical mitomycin-C for subepithelial fibrosis after refractive corneal surgery. Ophthalmology. 2000; 107(1):89-94.

73. Mohan RR, Hutcheon AEK, Choi RC et al. Apoptosis, necrosis, proliferation and myofibroblast generation in the stroma following LASIK and PRK. Experimental Eye Research 2003; 76(1):71-87. doi: 10.1016/S0014-4835(02)00251-8.

74. Jester JV, Petroll WM, Cavanagh HD. Corneal stromal wound healing in refractive surgery: the role of myofibroblasts. Prog Retin Eye Res. 1999; 18(3):311-56.

75. Moller-Pedersen T, Cavanagh HD, Petroll WM, Jester JV. Stromal wound healing explains refractive instability and haze development after photorefractive keratectomy: a 1-year confocal microscopic study. Ophthalmology 2000; 107(7):1235-45.

76. Pallikaris IG, Papatzanaki ME, Stathi EZ, Frenschock O, Georgiadis A. Laser in situ keratomileusis. Lasers Surg Med. 1990; 10(5):463-8.

77. Pallikaris IG, Papatzanaki ME, Siganos DS, Tsilimbaris MK. A corneal flap technique for laser in situ keratomileusis. Human studies. Arch Ophthalmol. 1991; 109(12):1699-702.

78. Buratto L, Ferrari M, Genisi C. Myopic keratomileusis with the excimer laser: one-year follow up. Refract Corneal Surg. 1993; 9(1):12-9.

79. Calvillo MP, McLaren JW, Hodge DO, Bourne WM. Corneal reinnervation after LASIK: prospective 3-year longitudinal study. Invest Ophthalmol Vis Sci. 2004; 45(11):3991–6. doi:10.1167/iovs.04-0561.

80. Donnenfeld ED, Ehrenhaus M, Solomon R et al. Effect of hinge width on corneal sensation and dry eye after laser in situ keratomileusis. J Cataract Refract Surg. 2004; 30(4): 790–7.

81. Kumano Y, Matsui H, Zushi I et al. Recovery of corneal sensation after myopic correction by laser in situ keratomileusis with a nasal or superior hinge. J Cataract Refract Surg. 2003; 29(4):757–61.

82. Hardten DR, Feder RS, Rosenfeld SI. Manual versus automated microkeratomes. In: Feder RS, Rapuano CJ, eds. The LASIK Handbook: A Case-Based Approach. Philadelphia: Lippincott Williams & Wilkins; 2007: pp 33–43.

83. Solomon KD, Donnenfeld E, Sandoval HP et al. Flap thickness accuracy: comparison of 6 microkeratome models. J Cataract Refract Surg. 2004; 30(5):964–77.

84. Lui MM, Silas MA, Fugishima H. Complications of photorefractive keratectomy and laser in situ keratomileusis. J Refract Surg. 2003; 19 (2 Suppl): S247-9.

85. Miyata K, Tokunaga T, Nakahara M et al. Residual bed thickness and corneal forward shift after laser in situ keratomileusis. J Cataract Refract Surg. 2004; 30:1067–72.

86. Schallhorn SC, Amersbury EC, Tanazer DJ. Avoidance, recognition, and management of LASIK complications. Am J Ophthalmol. 2006; 141(4):733-9.

87. Ambrósio R Jr, Wilson S. LASIK vs LASEK vs PRK: advantages and indications. Semin Ophthalmol. 2003; 18(1):2-10.

88. Sakimoto T, Rosenblatt MI, Azar DT. Laser eye surgery for refractive errors. Lancet. 2006; 367(9520):1432–47.

89. Moshirfar M, Gardiner JP, Schliesser JA et al. Laser in situ keratomileusis flap complica-tions using mechanical microkeratome versus femtosecond laser: retrospective comparison. J Cataract Refract Surg. 2010; 36(11):1925–33. doi: 10.1016/j.jcrs.2010.05.027.

90. Lackner B, Pieh S, Schmidinger G et al. Outcome after treatment of ametropia with implantable contact lenses. Ophthalmology. 2003; 110(11):2153-61.

91. El Danasoury MA, El Maghraby A, Gamali TO. Comparison of iris-fixed Artisan lens im-plantation with excimer laser in situ keratomileusis in correcting myopia between -9.00 and -19.50 diopters: a randomized study. Ophthalmology. 2002; 109(5):955–64.

92. Alberti KG, Zimmet P, Shaw J. Epidemiology Task Force Consensus Group The metabolic syndrome – a new worldwide definition. Lancet. 2005; 366(9491):1059–62.

93. Stulting RD, John ME, Maloney RK, Assil KK, Arrowsmith PN, Thompson VM. U.S. Verisyse Study Group. Three-year results of Artisan/Verisyse phakic intraocular lens implantation. Results of the United States Food And Drug Administration clinical trial. Ophthalmology. 2008; 115(3):464–72.

94. Joosse MV, Snoek C, van Minderhout HM. Comparison of wavefront-guided photorefractive keratectomy and foldable iris-fixated phakic intraocular lens implantation for low to moderate myopia. J Cataract Refract Surg.2011; 37(2):370–7. doi: 10.1016/j. jcrs.2010.08.051.

95. Izák M. Surgical trauma not lens design is responsible for myopia claw IOL Irritation. Ocular Surgery News. 1998;9:38.

96. Coullet J, Guëll JL, Fournié P et al. Iris-supported phakic lenses (rigid vs foldable version) for treating moderately high myopia: randomized paired eye comparison. Am J Ophthalmol. 2006; 142(6):909–16. DOI: 10.1016/j.ajo.2006.07.021.

97. Dick HB, Budo C, Malecaze F et al. Foldable Artiflex phakic intraocular lens for the correction of myopia: two-year follow-up results of a prospective European multicenter study. Ophthalmology. 2009; 116(4):671–7. doi: 10.1016/j.ophtha.2008.12.059.

98. Muñoz G, Cardoner A, Albarrán-Diego C, Ferrer-Blasco T, Belda-Salmerón L. Iris-fix-ated toric phakic intraocular lens for myopic astigmatism. J Cataract Refract Surg. 2012; 38(7):1166-75. doi: 10.1016/j.jcrs.2012.02.034.

99. Lee SY, Kwon HJ, Ahn HS, Seo KY, Kim EK, Kim TI. Comparison of patient outcomes after implantation of Visian toric implantable collamer lens and iris-fixated toric phakic intraocular lens. Eye (Lond). 2011; 25(11):1409-17. doi: 10.1038/eye.2011.176.

100. Ghoreishi M, Masjedi A, Nasrollahi K, Rahgozar A, Jenab K, Fesharaki H. Artiflex versus STAAR implantable contact lenses for correction of high myopia. Oman J Ophthal-mol. 2011; 4(3):116-9. doi: 10.4103/0974-620X.91266.

101. Savini G, Barboni P, Carbonelli M, Hoffer KJ. Agreement between Pentacam and video-keratography in corneal power assessment. J Refract Surg. 2009. 25(6): 534-8.

102. Symes RJ, Say MJ, Ursell PG. Scheimpflug keratometry versus conventional automated keratometry in routine cataract surgery. J Cataract Refract Surg. 2010; 36(7): 1107-14. doi: 10.1016/j. jcrs.2009.11.026.

103. Freitas GO, Boteon JE, Carvalho MJ, and Pinto RM. Treatment of astigmatism during phacoemulsification. Arq Bras Oftalmol. 2014; 77(1):40–6.

104. George D. Kymionis, MD, PHD. Correcting Astigmatism With the Excimer Laser. Refractive Surgery. SEP 2010.

105. Vinciguerra P, Epstein D, Azzolini M. Ablation of both meridians in LASIK and PRK- a new tissue saving strategy for correcting astigmatism. Invest Ophtalmol Vis Sci. 1999; 40:S782.

106. Chayet AS, Montes S, Gomez L, Rodriquez X, Robledo N, MacRae S. Bitoric laser in situ keratomileusis for the correction of simple myopic and mixed astigmatism. Ophthalmology. 2001; 108(2):303-8.

107. Epstein D, Vinciguerra P, Prussiani A, Camesasca FI. Cross-cylinder ablation in LASIK and PRK – A new tissue-sparing, accuracy-enhancing strategy for correcting astigmatism. Invest Ophtalmol Vis Sci. 2000; 41: S690.

108. Vinciguerra P, Camesasca FI, Urso R. Reduction of spherical aberration with the nidek NAVEX customized ablation system. J Refract Surg. 2003; 19(2 Suppl): S195-201.

109. Dausch D, Klein R, Landesz M, Schroder E. Photorefractive keratectomy to correct astigmatism with myopia or hyperopia. J Cataract Refract Surg. 1994; 20 Suppl: 252-7.

110. Azar DT, Primack JD. Theoretical analysis of ablation depths and profiles in laser in situ keratomileusis for compound hyperopic and mixed astigmatism. J Cataract Refract Surg. 2000; 26(8):1123-36.

111. Roberts C. Biomechanics of the cornea and wavefront-guided laser refractive surgery. J Refract Surg. 2002; 18(5): S589-92.

112. Chang J. Cyclotorsion during laser in situ keratomileusis. J Cataract Refract Surg. 2008; 34(10):1720-6. DOI: 10.1016/j.jcrs.2008.06.027.

113. Hori-Komai Y, Sakai C, Toda I et al. Detection of cyclotorsional rotation during excimer laser ablation in LASIK. J Refract Surg. 2007; 23(9):911-5.

114. Bharti S, Bains HS. Active cyclotorsion error correction during LASIK for myopia and myopic astigmatism with the NIDEK EC-5000 CX III laser. J Cataract Refract Surg. 2007; 23(9 Suppl):1041-5.

115. Ciccio AE, Durrie DS, Stahl JE, Schwendeman F. Ocular cyclotorsion during customized laser ablation. J Refract Surg. 2005; 21(6): S772-4.

116. Barraquer JI. The history and evolution of keratomileusis. Int Ophthalmol Clin. 1996; 36(4):1-7.

117. Vayr F, Chastang P, Hoang-Xuan T. Laser and mechanical microkeratomes. In: Azar DT, eds. Refractive Surgery. 2nd ed. Philadelphia: Elsevier Inc; 2007, p. 147-155.

118. Ratkay-Traub I, Ferincz IE, Juhasz T, Kurtz RM, Krueger RR. First clinical results with the femtosecond neodymium-glass laser in refractive surgery. J Refract Surg. 2003; 19(2):94–103.

119. Chung SH, Mazur E. Surgical applications of femtosecond laser. J Biophotonics. 2009; 2(10):557-72. doi: 10.1002/jbio.200910053.

120. Soong HK, Malta JB. Femtosecond lasers in ophthalmology. Am J Ophthalmol. 2009; 147(2):189–197. doi: 10.1016/j.ajo.2008.08.026.

121. Stern D, Schoenlein RW, Puliafito CA, Dobi ET, Birngruber R, Fujimoto JG. Corneal ablation by nanosecond, picosecond, and femtosecond lasers at 532 and 625 nm. Arch Ophthalmol. 1989; 107(4):587–92.

122. Barequet IS, Hirsh A, Levinger S. Effect of thin femtosecond LASIK flaps on corneal sensitivity and tear function. J Refract Surg. 2008; 24(9):897–902.

123. Sugar A. Ultrafast (femtosecond) laser refractive surgery. Curr Opin Ophthalmol 2002; 13(4):246-9.

124. Salomão MQ, Wilson SE. Femtosecond laser in laser in situ keratomileusis. J Cataract Refract Surg 2010; 36(6):1024-32.

125. Kymionis G, Kankariya V, Plaka A, Reinstein D. Femtosecond laser technology in corneal refractive surgery: A Review. J Refract Surg 2012; 28(12): 912-20. doi: 10.3928/1081597X-20121116-01.

126. Lubatschowski H. Overview of commercially available femtosecond lasers in refractive surgery. J Refract Surg 2008; 24:102-7.

127. Juhasz T, Kastis GA, Suárez C, Bor Z, Bron WE. Time-resolved observations of shock waves and cavitation bubbles generated by femtosecond laser pulses in corneal tissue and water. Lasers Surg Med 1996; 19(1):23-31.

128. Calvillo MP, McLaren JW, Hodge DO, Bourne WM. Corneal reinnervation after LASIK: prospective 3-year longitudinal study. Invest Ophthalmol Vis Sci. 2004; 45(11):3991–6.

129. Sonigo B, Iordanidou V, Chong-Sit D, Auclin F et al. In vivo corneal confocal microscopy comparison of Intralase femtosecond laser and mechanical microkeratome for laser in situ keratomileusis. Invest Ophthalmol Vis Sci. 2006; 47(7):2803-11.

130. Talamo JH, Meltzer J, Gardner J. Reproducibility of flap thickness with IntraLase FS and Moria LSK-1 and M2 microkeratomes. J Refract Surg. 2006; 22(6):556-61.

131. Kezirian GM, Stonecipher KG. Comparison of the IntraLase femtosecond laser and mechanical keratomes for laser in situ keratomileusis. J Cataract Refract Surg. 2004; 30(4):804-11.

132. Alió JL, Piñero DP. Very high-frequency digital ultrasound measurement of the LASIK flap thickness profile using the IntraLase femtosecond laser and M2 and Carriazo-Pendular microkeratomes. J Refract Surg. 2008; 24(1):12-23.

133. Nordan LT, Slade SG, Baker RN, Suarez C, Juhasz T, Kurtz R. Femtosecond laser flap creation for laser in situ keratomileusis: six-month follow-up of initial U.S. clinical series. J Refract Surg. 2003; 19(1):8-14.

134. Kim JY, Kim MJ, Kim TI, Choi HJ, Pak JH, Tchah H. A femtosecond laser creates a stronger flap than a mechanical microkeratome. Invest Ophthalmol Vis Sci. 2006; 47(2):599-604.

135. Binder PS. One thousand consecutive IntraLase laser in situ keratomileusis flaps. J Cataract Refract Surg 2006; 32(6):962-9.

136. Montés-Micó R, Rodríguez-Galietero A, Alió JL. Femtosecond laser versus mechanical keratome LASIK for myopia. Ophthalmology. 2007; 114(1):62-8.

137. Waring GO 3rd. Development of a system for excimer laser corneal surgery. Trans Am Ophthalmol Soc 1989; 87:854-983.

138. Manche EE, Carr JD, Haw WW, Hersh PS. Excimer laser refractive surgery. West J Med 1998; 169(1):30-38.

139. Puliafito CA, Steinert RF, Deutch TF et al. Excimer laser ablation of the cornea and lens: Experimental studies Ophthalmology 1985; 92:741-748.

140. Dehm EJ, Puliafito CA, Adler CM, Steinert RF. Corneal endothelial injury in rabbits following excimer laser ablation at 193 and 248 nm. Arch Ophthalmol 1986; 104:1364-8.

141. Garrison BJ, Srinivasan R. Microscopic model for the ablative photo decompensation of polymers by far ultraviolet radiation (193nm). Appl Phys Lett. 1984; 44:849-52.

142. Jellinek HH, Srinivasan R. Theory of etching of polymers by far-ultraviolet, high intensity pulsed laser and long term irradiation J Phys Chem 1984; 88:3048.

143. Kahle G, Stadter H, Seiler T et al. Gas chromatograph/mass spectrometer analysis of excimer and erbium Yag laser ablated human corneas. Invest Ophthalmol Vis Sci. 1992; 33(7): 2180-4.

144. Nuss RC, Puliafito CA, Dehm EJ. Unscheduled DNA synthesis following excimer laser ablation of the comea in vivo. Invest Ophthalmol Vis Sci. 1987; 28:287-94.

145. Kochevar IE. Cytotoxicity and mutagenicity of excimer laser radiation. Lasers Surg Med 1989; 9(5):440-5.

146. Chastang P, Vayr F, Hoang-Xuan. Excimer lasers. In: Azar DT, eds. Refractive Surgery. 2nd ed. Philadelphia: Elsevier Inc; 2007, p. 157-163.

147. Moreno-Barriuso E, Lloves JM, Marcos S, Navarro R, Llorente L, Barbero S. Ocular aberrations before and after myopic corneal refractive surgery: LASIK-induced changes measured with laser ray tracing. Invest Ophthalmol Vis Sci. 2001; 42(6):1396-403.

148. Oshika T, Klyce SD, Applegate RA, Howland HC, El Danasoury MA. Comparison of corneal wavefront aberrations after photorefractive keratectomy and laser in situ keratomileusis. Am J Ophthalmol. 1999; 127(1):1-7.

149. Liang J, Williams DR, Miller DT. Supernormal vision and high resolution retinal imaging through adaptive optics. J Opt Soc Am A Opt Image Sci Vis. 1997; 14:2884–2892.

150. Mrochen M, Kaemmerer M, Seiler T. Wavefront guided laser in situ keratomileusis: early results in three eyes. J Refract Surg. 2000; 16(2):116–121.

151. Kohnen T, Bühren J, Kühne C, Mirshahi A. Wavefront-guided LASIK with the Zyoptix 3.1 system for the correction of myopia and compound myopic astigmatism with 1-year follow-up: clinical outcome and change in higher order aberrations. Ophthalmology. 2004; 111(12):2175-85.

152. Zhou C, Chai X, Yuan L, He Y, Jin M, Ren Q. Corneal higher-order aberrations after customized aspheric ablation and conventional ablation for myopic correction. Curr Eye Res. 2007; 32(5):431-8.

153. Randleman JB, Perez-Straziota CE, Hu MH, White AJ, Loft ES, Stulting RD. Higher-order aberrations after wavefront-optimized photorefractive keratectomy and laser in situ ker-atomileusis. J Cataract Refract Surg. 2009; 35:260–4.

154. Kulkamthorn T, Silao JN, Torres LF et al. Wavefront-guided laser in situ keratomileusis in the treatment of high myopia by using the CustomVue wavefront platform. Cornea. 2008; 27(7):787-90. doi: 10.1097/ICO.0b013e31816a3554.

155. Chalita MR, Chavala S, Xu M, Krueger RR. Wavefront analysis in post-LASIK eyes and its correlation with visual symptoms, refraction, and topography. Ophthalmology. 2004; 111(3):447–53.

156. Bühren J, Martin T, Kühne A, Kohnen T. Correlation of aberrometry, contrast sensitivity, and subjective symptoms with quality of vision after LASIK. J Refract Surg. 2009; 25(7):559–68.

157. Yamane N, Miyata K, Samejima T, et al. Ocular higher-order aberrations and contrast sensitivity after conventional laser in situ keratomileusis. Invest Ophthalmol Vis Sci. 2004; 45(11):3986–90.

158. Stonecipher KG, Kezirian GM, Stonecipher K. LASIK for mixed astigmatism using the ALLEGRETTO WAVE. 3-and-6-month results with 200- and 400-Hz platforms. J Refract Surg. 2010; 26(10):819–823. doi: 10.3928/1081597X-20100921-09.

159. Stonecipher KG, Kezirian GM. Wavefront-optimized versus wavefront-quided LASIK for myopic astigmatism with the Allegretto Wave: Three-month results of a prospective FDA Trial. J Refract Surg. 2008; 24(4):424–30.

160. De Ortueta D, Arba Mosquera S, Baatz H. Comparison of standard and aberration-neutral profiles for myopic LASIK with the SCHWIND ESIRIS platform. J Refract Surg. 2009; 25(4):339-49.

161. Arbelaez MC, Aslanides IM, Barraquer C, et al. LASIK for myopia and astigmatism using the SCHWIND AMARIS excimer laser: an international multicenter trial. J Refract Surg. 2010; 26(2):88-98. doi: 10.3928/1081597X-20100121-04.

162. Arba Mosquera S, Merayo-Lloves J, de Ortueta D. Clinical effects of pure cyclotorsional errors during refractive surgery. Invest Ophthalmol Vis Sci. 2008; 49(11):4828-36. doi: 10.1167/iovs.08-1766.

163. Alió JL, Rosman M, Arba-Mosquera S (2010) Minimally invasive refractive surgery. In: Fine H, Mojon D (eds) Minimally invasive ophthalmic surgery. Springer, Berlin, pp 97–122.

164. Arbelaez MC, Vidal C, Jabri BA, Arba Mosquera S. LASIK for myopia with Aspheric “aberration neutral” ablations using the ESIRIS laser system. J Refract Surg. 2009; 25(11):991-9. doi: 10.3928/1081597X-20091016-04.

165. Arba-Mosquera S, de Ortueta D. Analysis of optimized profiles for “aberration-free” refractive surgery. Ophthalmic Physiol Opt. 2009 Sep; 29(5):535-48. doi: 10.1111/ j.1475-1313.2009.00670.

166. Munnerlyn CR, Koons SJ, Marshall J. Photorefractive keratectomy: a technique for laser refractive surgery. J Cataract Refract Surg. 1988; 14(1):46-52.

167. Reinstein DZ, Carp GI, Lewis TA, Archer TJ, Gobbe M. Outcomes for Myopic LASIK With the MEL 90 excimer laser. J Refract Surg. 2015; 31(5):316-21. doi: 10.3928/1081597X-20150423-05.

168. Khalifa MA, Mossallam EF, Massoud TH, Shaheen MS. Comparison of visual outcomes after variable spot scanning ablation versus wavefront-optimized myopic LASIK. J Refract Surg. 2015; 31(1):22-8. doi: 10.3928/1081597X-20141218-03.

169. Abbott Medical Optics [homepage on the internet] Star S4 IR Excimer laser. [Citated 12 October 2015]. Available on: http://www.abbottmedicaloptics.com/products/refractive/ ilasik/star-s4-ir-excimer-laser

170. Han DC, Chen J, Htoon HM, Tan DT, Mehta JS. Comparison of outcomes of conventional WaveLight Allegretto Wave and Technolas excimer lasers in myopic laser in situ keratomileusis. Clin Ophthalmol. 2012; 6:1159-68.

171. Shaikh NM, Manche EE. Laser in situ keratomileusis for myopia and compound myopic astigmatism using the Technolas 217 scanning spot laser. J Cataract Refract Surg 2002; 28(3):485-490.

172. Bausch & Lomb/Technolas [homepage on the internet]. Technolas Excimer Workstation 217P Technical Specifications. [Cited on 12th of October 2015]. Available on: http://tech-nolaspv.com/ dasat/images/3/100643-technolas-217p-070911-update-blt.pdf

173. Nidek [homepage on the internet]. Topo-Assisted Excimer Laser. [Cited on 12th of October 2015]. Available on: http://usa.nidek.com/products/excimer-laser

174. Peter K. Kaiser, Prospective Evaluation of Visual Acuity Assessment: A Comparison of Snellen Versus ETDRS Charts in Clinical Practice (An AOS Thesis). Trans Am Ophthalmol Soc. 2009 Dec; 107:311–324.

175. Dai GM (2008) Wavefront transformation and iris registration. In: Dai GM (ed) Wavefront optics for vision correction. SPIE Press, Bellingham, pp 168–171.

176. De Ortueta D, Schreyger FD. Centration on the corneal vertex normal during hyperopic refractive photoablation using videokeratoscopy. J Refract Surg. 2007; 23(2):198–200.

177. Alió JL, Pachkoria K, El Aswad A, Plaza-Puche AB. Laser-assisted in situ keratomileusis in high mixed astigmatism with optimized, fast-repetition and cyclotorsion control excimer laser. Am J Ophthalmol. 2013; 155(5):829-36. doi: 10.1016/j.ajo.2012.11.027.

178. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. Optom Vis Sci 1997; 74(6):367–75.

179. Miller JM. Clinical applications of power vectors. Optom Vis Sci. 2009 Jun; 86(6):599-602. doi: 10.1097/OPX.0b013e3181a6a211.

180. Thibos LN, Horner D. Power vector analysis of the optical outcome of refractive surgery. J Cataract Refract Surg. 2001; 27(1):80-5.

181. Koshy JJ, Nishi Y, Hirnschall N, et al. Rotational stability of a single-piece toric acrylic intraocular lens. J Cataract Refract Surg. 2010; 36(10):1665-70. doi: 10.1016/j. jcrs.2010.05.018.

182. Statham M, Apel A, Stephensen D. Comparison of the AcrySof SA60 spherical intraocular lens and the AcrySof Toric SN60T3 intraocular lens outcomes in patients with low amounts of corneal astigmatism. Clin Exp Ophthalmol. 2009; 37(8):775-9. doi: 10.1111/ j.1442-9071.2009.02154.

183. Mingo-Botín D, Muñoz-Negrete FJ, Won Kim HR, Morcillo-Laiz R, Rebolleda G, Oblanca N. Comparison of toric intraocular lenses and peripheral corneal relaxing incisions to treat astigmatism during cataract surgery. J Cataract Refract Surg. 2010; 36(10):1700-8. doi: 10.1016/j.jcrs.2010.04.043

184. Koch DA. Excimer laser technology: new options coming to fruition. J Cataract Refract Surg. 1997; 23(10):1429-30.

185. Koch DD. Reporting astigmatism data. J Cataract Refract Surg. 1998; 24(12):1545.

186. Koch DD. Astigmatism analysis: the spectrum of approaches. J Cataract Refract Surg. 2006; 32(12):1977- 8.

187. Alpins, NA, Goggin, M. Practical astigmatism analysis for refractive outcomes in cataract and refractive surgery. Surv Ophthalmol. 2004; 49 (1): 109 22.

188. Freitas GO, Boteon JE, Carvalho J, Pinto R. Alpins and Thibos vectorial astigmatism analyses – proposal of a linear regression model between methods. Rev Bras Oftalmol. 2013. 72(5):307-11.

189. Ambrósio R Jr, Jardim D, Netto MV, Wilson SE. Management of unsuccessful LASIK sur-gery. Compr Ophthalmol Update 2007; 8(3):125-41.

190. Hammond MD, Madigan WP Jr, Bower KS. Refractive surgery in the United States Army, 2000-2003. Ophthalmology 2005; 112(2):184-90.

191. Chen S, Feng Y, Stojanovic A, Jankov MR 2nd, Wang Q. IntraLase femtosecond laser vs mechanical microkeratomes in LASIK for myopia: a systematic review and meta-analysis. J Refract Surg 2012; 28(1):15–24. doi: 10.3928/1081597X-20111228-02.

192. Patel SV, Maguire LJ, McLaren JW, Hodge DO, Bourne WM. Femtosecond lasers versus mechanical microkeratome for LASIK: a randomized controlled study. Ophthalmology 2007; 114(8):1482-90.

193. Lim T, Yang S, Kim M, Tchah H. Comparison of the IntraLase femtosecond laser and mechanical microkeratome for laser in situ keratomileusis. Am J Ophthalmol 2006; 141(5):833-9.

194. Wong RC, Yu M, Chan TC, Chong KK, Jhanji V. Longitudinal comparison of outcomes after sub-Bowman keratomileusis and laser in situ keratomileusis: randomized, double-masked study. Am J Ophthalmol. 2015; 159(5):835-45. doi: 10.1016/j.ajo.2015.02.003.

195. Cosar CB, Gonen T, Moray M, Sener AB. Comparison of visual acuity, refractive results and complications of femtosecond laser with mechanical microkeratome in LASIK. Int J Ophthalmol. 2013; 6(3):350-5. doi: 10.3980/j.issn.2222-3959.2013.03.18.

196. Varley GA, Huang D, Rapuano CJ, Schallhorn S, Boxer Wachler BS, Sugar A. LASIK for hyperopia, hyperopic astigmatism and mixed astigmatism, a report by American Academy of Ophthalmology. Ophthalmology. 2004; 111:1604-17.

197. Salz JJ, Stevens CA, LADARVision LASIK Hyperopia Study Group. LASIK correction of spherical hyperopia, hyperopic astigmatism, and mixed astigmatism with the LADARVision excimer laser system. Ophthalmology. 2002; 109(9):1647–56.

198. Ganesh S, Brar S, Pawar A. Matched population comparison of visual outcomes and patient satisfaction between 3 modalities for the correction of low to moderate myopic astigmatism. Clin Ophthalmol. 2017; 11:1253-1263. doi: 10.2147/OPTH.S127101.

199. Davis EA, Lindstrom RL. Astigmatism management: ablation patterns. Curr Opin Ophthalmol. 2001; 12:300-303.

200. Binder PS, Rosenshein J. Retrospective comparison of 3 laser platforms to correct myopic spheres and spherocylinders using conventional and wavefront-guided treatments. J Cataract Refract Surg. 2007; 33(7):1158–76.

201. Hori-Komai Y, Toda I, Asano-Kato N, Ito M, Yamamoto T, Tsubota K. Comparison of LASIK using the NIDEK EC-5000 optimized aspheric transition zone (OATz) and conventional ablation profile. J Refract Surg. 2006; 22(6):546–55.

202. Ambrósio R Jr, Wilson SE. Complications of laser in situ keratomileusis: etiology, prevention, and treatment. J Refract Surg. 2001; 17(3):350-79.

203. Melki SA, Azar DT. LASIK complications: etiology, management, and prevention. Surv Ophthalmol 2001; 46(2):95-116.

204. Dupps WJ, Wilson SE. Biomechanics and wound healing in the cornea. Exp Eye Res. 2006; 83(4):709-20.

205. Rueda L, Pineda-Fernández A, Huang D, Nur J. Laser in situ keratomileusus for mixed and simple myopic astigmatism with the Nidek EC-5000 Laser. J Refract Surg. 2002; 18(3):234-8.

206. Moshirfar M, Betts SB, Churgin DS, et al. A prospective, randomized, fellow eye comparison of WaveLight Allegretto Wave Eye-Q versus VISX CustomVue STAR S4 IR in laser in situ keratomileusis (LASIK): analysis of visual outcomes and higher order aberrations. Clin Ophthalmol. 2011; 5:1339–47. doi: 10.2147/OPTH.S24316.

207. Ziaei M, Mearza AA, Allamby D. Wavefront-optimized laser in situ keratomileusis with the Allegretto Wave Eye-Q excimer laser and the FEMTO LDV Crystal Line femtosecond laser: 6 month visual and refractive results. Cont Lens Anterior Eye. 2015; 38(4)245-9. doi:10.1016/j.clae.2015.02.004.

208. Tomita M, Watabe M, Yukawa S, Nakamura N, Nakamura T, Magnago T. Safety, efficacy, and predictability of laser in situ keratomileusis to correct myopia or myopic astigmatism with a 750 Hz scanning-spot laser system. J Cataract Refract Surg. 2014;40(2):251-8. doi: 10.1016/j.jcrs.2013.07.043.

209. Myopia or myopic astigmatism with a 750 Hz scanning-spot laser system. J Cataract Refract Surg. 2014; 40(2):251-8. doi: 10.1016/j.jcrs.2013.07.043.

210. Kilavuzoğlu AE, Gönen T, Çelebi AR, Coşar Yurteri CB, Şener AB. Treatment of mixed astigmatism: early clinical outcomes with WaveLight and Technolas excimer lasers. Turk J Med Sci. 2016; 9; 46(3):664-72. doi: 10.3906/sag-1504-35.

211. Alió JL, Plaza-Puche AB, Martinez LM, Torky M, Brenner LF. Laser in situ keratomileusis using optimized aspheric profiles and cyclotorsion control to treat compound myopic astigmatism with high cylinder. J Cataract Refract Surg. 2013; 39(1):28–35. doi: 10.1016/j. jcrs.2012.07.037

212. Lui MM, Silas MA, Apelbaum B, Oshima A. Laser in situ keratomileusis with the Nidek EC-5000 excimer laser for astigmatism greater than 4.00 D. J Refract Surg. 2002; 18(3 Suppl): S321-2.

213. Alió JL, Soria F, Abbouda A, Peña-García P. Laser in situ keratomileusis for -6.00 to -18.00 diopters of myopia and up to -5.00 diopters of astigmatism: 15-year follow-up. J Cataract Refract Surg. 2015; 41(1):33-40. doi: 10.1016/j.jcrs.2014.08.029.

214. Pinelli R, Ngassa EN, Scaffidi E. Sequential ablation approach to the correction of mixed astigmatism. J Refract Surg. 2006; 22(8):787–94.

215. De Ortueta D, Haecker C. Laser in situ keratomileusis for mixed astigmatism using a modified formula for bitoric ablation. Eur J Ophthalmol. 2008; 18(6):869-76.

216. April 1, 2009 Ophthalmology Times reported on a study Dr. Kerry Solomon on LASIK satisfaction. Calgary LASIK, Epi-LASIK, PRK: Patient Satifaction. April 22, 2009. Available at http:/www.westernlasereye.com/calgary-lasik-epi-lasik-prk-patient-satisfaction/

217. Teus MA, Arruabarrena C, Hernández-Verdejo JL, Cañones R, and Mikropoulos DG. Ocular residual astigmatism's effect on high myopic astigmatism LASIK surgery. Eye (Lond). 2014; 28(8): 1014–9. doi: 10.1038/eye.2014.133.

218. Abolhassani A, Shojaei A, Baradaran-Rafiee AR, Eslani M, Elahi B, Noorizadeh F. Vector analysis of cross cylinder LASIK with the NIDEK EC-5000 excimer laser for high astigmatism. J Refract Surg. 2009; 25(12):1075–82. doi: 10.3928/1081597X-20091117-06.

219. Alpins NA. A new method of analyzing vectors for changes in astigmatism. J Cataract Re-fract Surg. 1993; 19:524–533.

220. Duncombe KO. A new and remarkably sensitive test for astigmatism. Br J Physiol Optics. 1933; 7:112–1128.

221. Links A. Determination of axis and amount of astigmatic error by rotation of trial cylinder. Arch Ophthalmic. 1942; 28:632–651.

222. Fearn WWL. The effect of axis errors on prescription comfort. Optician. 1948; 115:355–7.

223. Anderson FR. To tilt or not to tilt: a controversy rehashed. Surv Ophthalmol. 1969; 14:55– 60.

224. Guyton DL. Prescribing cylinders: the problem of distortion. Surv Ophthalmol. 1977; 22(3):177–188.

225. Retzlaff J, Paden PY, Ferrell L. Vector analysis of astigmatism. Adding and substracting spherocylinders. J Cataract Refract Surg. 1993; 19(3):393–8.

226. Jennings JAM, Charman WN. A comparison of errors in some methods of subjective refraction. Ophthalmic Optician. 1973; 13:11–18.

227. Rosenfield M, Chiu NN. Repeatability of subjective and objective refraction. Optom Vis Sci. 1995; 72(8):577–9.

228. Leinonen J, Laakkonen E, Laatikainen L. Repeatability (test-retest variability) of refractive error measurement in clinical settings. Acta Ophthalmol Scand. 2006; 84(4):532–6. doi:10. 1111/j.1600-0420.2006.00695.

229. Schallhorn SC, Farjo AA, Huang D, et al. Wavefront-guided LASIK for the correction of primary myopia and astigmatism a report by the American Academy of Ophthalmology. Ophthalmology. 2008; 115(7):1249–61.

230. Ivarsen A, Naeser K, Hjortdal J. Laser in situ keratomileusis for high astigmatism in myopic and hyperopic eyes. J Cataract Refract Surg. 2013; 39 (1):74–80. doi: 10.1016/j. jcrs.2012.08.054.

231. Katz T, Wagenfield L, Galambos P, Darrelman BG, Richard G, Linke SJ. LASIK versus photorefractive keratectomy for high myopic (>3 diopter) astigmatism. J Refract Surg. 2013; 29(12):824–31. doi:10.3928/1081597X-20131029-03.

232. Morlet N, Minassian D, Dart J. Astigmatism and the analysis of its surgical correction. Br J Ophthalmol. 2001; 85(9):1127–38.

233. Alpins N. Astigmatism analysis by the Alpins method. J Cataract Refract Surg 27(1):31-49.

234. McCormick GJ, Porter J, Cox IG, MacRae S. Higher-order aberrations in eyes with irregular corneas after laser refractive surgery. Ophthalmology. 2005; 112(10):1699–1709.

235. Oshika T, Okamoto C, Samejima T, Tokunaga T, Miyata K. Contrast sensitivity function and ocular higher-order wavefront aberrations in normal human eyes. Ophthalmology. 2006; 113(10):1807–12.

236. Applegate RA, Sarver EJ, Khemsara V. Are all aberrations equal? J Refract Surg. 2002; 18(5):556–62.

237. Alpins N, Ong JK, Stamatelatos G. Refractive surprise after toric intraocular lens implantation: graph analysis. J Cataract Refract Surg. 2014; 40(2):283–94. doi: 10.1016/j. jcrs.2013.06.029.

238. Krall EM, Arlt EM, Hohensinn M, et al. Vector analysis of astigmatism correction after toric intraocular lens implantation. J Cataract Refract Surg. 2015; 41:790–9.

239. Emsley HB (1972) Visual optics, vol. 1. 5th edition. Butterworths, Edinburgh, p 154.

11. CURRICULUM VITAE

Alma Biščević, MD, ophthalmology specialist

I was born on August 26th 1982 in Belgrade, Serbia. I graduated from School of Medicine, University of Sarajevo in 2008. In 2009 I started PhD programme Biomedicine and Health sciences at School of Medicine, University of Zagreb, and in 2015 defended the thesis proposal with title ''Prospective comparison of two excimer laser platforms in treatment of high astigmatism with laser in situ keratomileusis'' under the mentorship of Prof. Iva Dekaris, MD, PhD.

I finished Specialist postgraduate study of Ophthalmology and Optometry at School of Medicine, University of Zagreb in 2014. Since 2010 I work at University Eye Hospital Svjetlost in Zagreb, first as a resident and from 2014 as ophthalmology specialist. I attended several educations and trainings abroad, with a focus on the front eye segment, refractive surgery, corneal transplantation and regularly participate at domestic and international ophthalmology meetings as a speaker. So far I published 3 scientific papers in journals indexed in Current Contents, and more than 30 congress abstracts. I am a member of European Society for Cataract and Refractive Surgery (ESCRS), South East European Ophtalmological Society (SEEOS), European Eye Bank Association (EEBA) and Croatian Society for cataract and Refractive Surgery (CSCRS).