

# Presbyopia treatment by lens surgery versus Laser in situ keratomileusis

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**Doctoral thesis / Disertacija**

**2021**

*Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj:* **University of Zagreb, School of Medicine / Sveučilište u Zagrebu, Medicinski fakultet**

*Permanent link / Trajna poveznica:* <https://urn.nsk.hr/urn:nbn:hr:105:667565>

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**UNIVERSITY OF ZAGREB**

**SCHOOL OF MEDICINE**

**Adis Pašalić**

**Presbyopia treatment by lens surgery versus  
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**DISSERTATION**



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Dissertation was fully conducted at the 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 mentors Prof. Iva Dekaris, MD, PhD and Prof. Nikica Gabrić MD, PhD for their 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 coworkers and friends Alma Bišćević MD, PhD and Nataša Drača MD, PhD for their help in study conduction and critical evaluation of the data and final work. In addition, I would like to say thank you to all my colleagues for all their help in patient selection and data collection.*

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

*And finally, my special thanks go to my late mother, this is for her.*

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## LIST OF ABBREVIATIONS

*mm.....millimeter*

*μm .....micrometer*

*% .....percent*

*D .....diopter*

*m..... meter*

*AL.....axial length*

*VA.....visual acuity*

*cm..... centimeter*

*J..... Jaeger*

*RGP.....rigid gas permeable*

*RLE.....refractive lens exchange*

*IOL.....intraocular lens*

*MFIOL.....multifocal intraocular lens*

*UNVA..... uncorrected near visual acuity*

*UDVA.....uncorrected distance visual acuity*

*UIVA..... uncorrected intermediate visual acuity*

*EDOF.....enhanced depth of focus*

*C.....Celsius*

*CK..... conductive keratoplasty*

*kHz.....kilohertz*

*Hz ..... hertz*

*LASIK .....Laser in situ keratomileusis*

*LVC.....laser vision correction*

*nm..... nanometer*

*mJ.....millijoule*

*cm<sup>2</sup> .....square centimeter*

*s.....second*

*IOP.....intraocular pressure*

*BCDVA..... best corrected distance visual acuity*

*BCNVA..... best corrected near visual acuity*

*pIOL.....phakic intraocular lens*

*UV-C.....ultraviolet short wave*

*ns.....nanosecond*

*SE.....spherical equivalent*

*MAR.....minimum angle of resolution*

*CS..... contrast sensitivity.*



## 1. INTRODUCTION

Vision is by far the most used of the five senses and is one of primary means that we use to gather information from our surroundings. More than 75% of the information we receive about the world around us consists of visual information. Vision is our window to the outside world.

Refractive errors are a common, correctable cause of impaired vision throughout the world. The normal eye creates a clear image by bending (refracting) light to focus onto the retina. Refractive errors occur when a component of the eyes optical system fails to focus the optical image. Causes of refractive errors include aberrations in the shape of the cornea, length of the eyeball and reduced flexibility of the lens.

These anomalies can mostly be corrected by optical means (such as eyeglasses, contact lenses, refractive surgery, etc.).

### 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 horizontal diameter of the cornea typically measures about 12 millimeters (mm), and the vertical diameter is 11 millimeters. The axial thickness of the cornea ranges from 0.50 to 0.52 millimeters, Center thickness of the average cornea is about 550 microns ( $\mu\text{m}$ ). The cornea has five histological layers.

From front to back, these layers are:

1. The corneal epithelium. This outer layer of the cornea is five to seven cells thick and measures about 50 microns, making it slightly less than 10 percent (%) of the thickness of the entire cornea. Epithelial cells are constantly being produced and sloughed off in the tear layer of the surface of the eye. The turnover time for the entire corneal epithelium is about one week.

2. Bowman's layer. This is a very thin (8 to 14 microns) and dense fibrous sheet of connective tissue that forms the transition between the corneal epithelium and the underlying stroma.
3. The corneal stroma. This middle layer of the cornea is approximately 500 microns thick, or about 90 percent of the thickness of the overall cornea. It is composed of strands of connective tissue called collagen fibrils. These fibrils are uniform in size and are arranged parallel to the cornea surface in 200 to 300 flat bundles called lamellae that extend across the entire cornea. The regular arrangement and uniform spacing of these lamellae is what enables the cornea to be perfectly clear.
4. Descemet's membrane. This very thin layer separates the stroma from the underlying endothelial layer of the cornea. Descemet's membrane gradually thickens throughout life and it's about 5 microns thick in children and 15 microns thick in older adults.
5. The corneal endothelium. This is the innermost layer of the cornea. The back of the endothelium is bathed in the clear aqueous humor that fills the space between the cornea and the iris and pupil. The corneal endothelium is only a single layer of cells thick and measures about 5 microns. Most of the endothelial cells are hexagonal (six-sided). The regular arrangement of these cells is sometimes called the endothelial mosaic.<sup>1-3</sup>

The 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).

When light passes through the cornea, it goes through the pupil that is controlled by the iris and then it passes through flexible crystalline lens that focuses light on the retina. The lens has no blood supply or innervation after fetal development, and it depends entirely on the aqueous humor to meet its metabolic requirements and to carry off its wastes. It lies posterior to the iris and anterior to the vitreous body. The lens is suspended in position by the zonules of Zinn, which consist of delicate yet strong fibers that support and attach it to the ciliary body. The lens is composed of the capsule, lens epithelium, cortex and nucleus.

On the way to the retina, light also passes through the interior of the eye that is filled with gel fluid called corpus vitreous. The retina converts the light into nerve impulses which are carried by neurons to the vision centers in the brain and there they get interpreted so that we can see.<sup>4</sup>

## **1.2. FUNCTIONAL ANATOMY OF THE EYE**

Functional anatomy of the eye presents the eye's ability to focus, which is dependent on the eye's optical system, consisting of two refractive surfaces working in tandem: the cornea and the crystalline lens.

The cornea is the more powerful refractive element, accounting for two thirds of the eye's refractive power. The lens provides the remaining one third, for a total refractive power of 60D. Refractive power of the eye and corrective lenses is measured in diopters, where a diopter is the reciprocal of the focal length measured in meters (m). The focal length is the distance from a lens to its focus or focal point.

The cornea has a fixed amount of refractive power, while the lens can vary its power by altering its shape. Accommodation is the term used to describe this change in lens shape, which can increase the power of the lens to enable the eye to focus on objects at arm's length or closer.<sup>5</sup>

Refractive error is a problem with focusing light accurately onto the retina due to the shape of the eye. The most common types of refractive error are nearsightedness and farsightedness. Nearsightedness results in distant objects being blurry, whereas farsightedness and presbyopia result in close objects being blurry, astigmatism causes objects to appear stretched out or blurry.<sup>6</sup>

An eye that has no refractive error when viewing distant objects is said to have emmetropia or to be emmetropic, meaning the eye is in a state in which it can focus parallel rays of light (light from distant objects) on the retina, without using any accommodation. A distant object in this case is defined as an object located beyond 6 meters from the eye, since the light from those objects arrives as essentially parallel rays when considering the limitations of human perception.<sup>7</sup>

### **1.2.1. DEFINITIONS OF REFRACTIVE ERRORS**

Emmetropia (normal refraction) describes state of refraction in which parallel light rays emanating from an object located 6 meters or more from the eye, form a focused image on the retina of an eye that has not accommodated.

Myopia (nearsightedness) is a common refractive disorder in which the axial length (AL) of the eye is either too long (axial length is the distance from the posterior corneal surface to the retina) or the refractive power of the eye's optical system is too great (generally due to a steep cornea). The image is therefore focused in front of the retina. This results in blurred distance vision, unless optical correction is achieved with a refractive device or surgery. Some of the signs and symptoms of nearsightedness include: difficulty seeing objects in distant such as road signs, eyestrain, headaches, squinting to see properly.<sup>8</sup>

Hyperopia (farsightedness) is a refractive disorder in which the axial length of the eye is too short or the power of the eye's optical system is insufficient (due to a flat cornea) to produce a focused image on the retina. The image is then focused behind the retina. Hyperopia is corrected either with a refractive device that provides a more convex refracting surface in order to increase the deficient focusing power of the eye's optical system, or surgical procedures. Farsighted people may have symptoms such as headaches or may squint or often feel fatigued when performing work at close range. Sometimes people confuse hyperopia with presbyopia (that comes with age), which also causes near vision problems but with different onset mechanism.

Astigmatism refers to the refractive condition in which a warped corneal surface causes light rays entering the eye along different planes to be focused unevenly. The patient reports blurred vision at all viewing distances. Astigmatism is corrected by spectacles containing a cylindrical optical surface or surgery. Astigmatism is usually present from birth, may develop following an eye injury or eye surgery. It also can occur due to a relatively rare condition called keratoconus in which the cornea becomes progressively thinner and cone-shaped. Astigmatism has three primary classifications, defined by the principal meridians (the steepest and flattest meridians of the eye): myopic astigmatism (principal meridians of the eye are nearsighted),

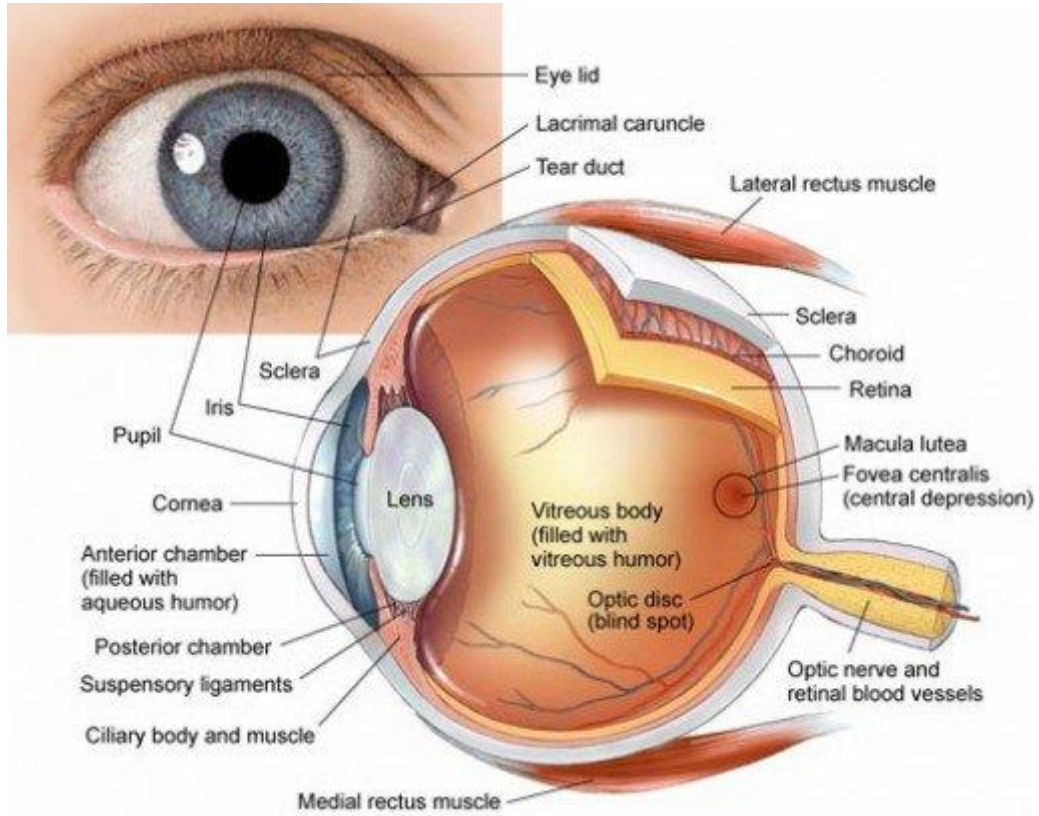
hyperopic astigmatism (principal meridians of the eye are farsighted), and mixed astigmatism (principal meridians are both near and farsighted).

Presbyopia (aging sight) is a refractive error that also affects visual acuity (VA). It is the normal loss of near focusing ability that occurs with age, most people begin to notice that after the age of 40 years, when they start having trouble seeing small print clearly. Presbyopia occurs when the lens loses its normal accommodating power and can no longer focus on objects viewed at arm's length or closer. As such, it is not considered an emmetropic state, but rather one, in which the normal physiologic function of lens accommodation has been lost. It is often a significant and emotional event because it is a sign of aging that is impossible to ignore and difficult to hide and reduces quality of life and productivity. Symptoms of presbyopia is holding reading material farther from your eyes to see them more clearly, eye strain, headaches or visual fatigue from doing close work.

In youth, the eye is able to easily accommodate or increase the curvature of the lens by contracting the ciliary muscle. The ciliary muscle surrounds the lens and is connected to it by zonular fibers. The normally taut zonular fibers stretch the lens and keep it from assuming a fully rounded state. The desire to focus on reading material automatically stimulates ciliary smooth muscle contraction, which loosens the zonular fibers and allows the lens to become more rounded. In the fully rounded state, the lens provides the additional refractive power needed to bring reading material into focus.

During the natural aging process, the crystalline lens loses its elasticity and therefore its ability to become more rounded when the zonular fibers loosen their grip.<sup>9</sup>

Figure 1. Anatomy of the eye



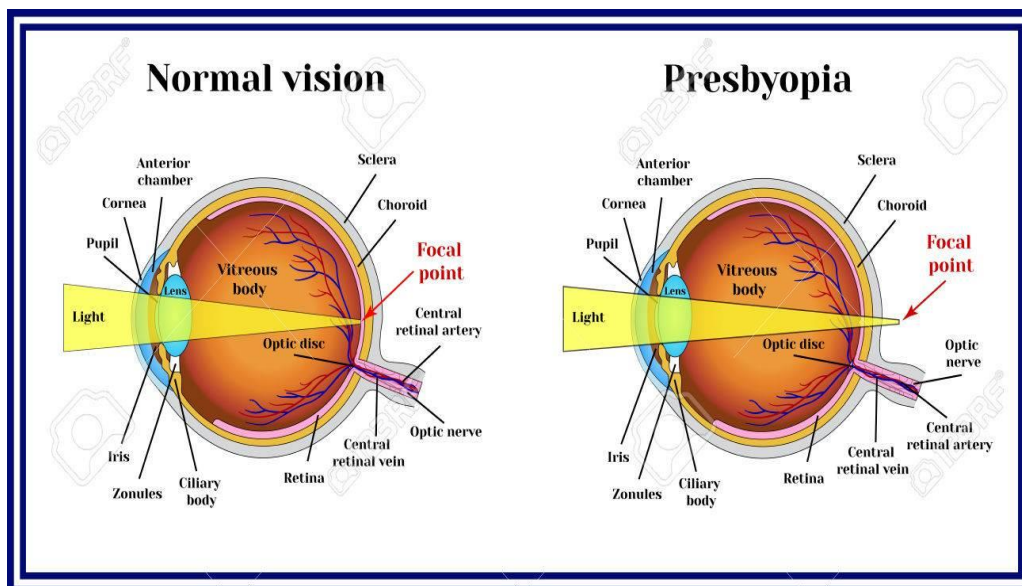
Courtesy of Dave Carlson / CarlsonStockArt.com

### 1.3. PRESBYOPIA

Presbyopia is the most common refractive error, currently affecting approximately 2 billion people worldwide, with a predicted steep rise to 2.1 billion in 2020.<sup>10,11</sup>

Presbyopia itself is defined as an age-related loss of accommodation of the crystalline lens. This condition typically manifests in people over the age of 40 years and can contribute to a considerable decrease in the quality of life for many of those affected. The ability to focus on near objects declines throughout life, from an accommodation of about 20 diopters in child, to 10 diopters at the age 25, and levels off at 0.5 to 1 diopter at the age 60 (ability to focus down to 1-2 meters only).<sup>12,13</sup>

Figure 2. Anatomy of the eye, normal vision and presbyopia



Courtesy of Dave Carlson / CarlsonStockArt.com

Presbyopia is a global problem affecting people worldwide, with the number of people with presbyopia set to increase further against a backdrop of an ageing global population where the median age could reach age of 40 years by 2050 (the median age of the world population in 2015 was 29.6 years).<sup>14,15</sup>

In the younger human eye, the accommodation mechanism acts to enable individuals to view targets clearly at various distances. Although there are ongoing debates as to the exact mechanism of accommodation, the most compelling empirical data support Helmholtz's theory where, in a response to ciliary muscle contraction, crystalline lens thickness increases lens diameter decreases and both the anterior and posterior curvature of the lens increase resulting in an increase in lenticular power and, therefore, accommodation.<sup>16-23</sup>

Some definitions of presbyopia purely focus on near visual loss, but do not relate this to a visual requirement hence, many young visually impaired individuals could be considered by such definitions as presbyopia affected. However, other definitions are more functional, such as: "presbyopia is a condition of age rather than ageing and, as such, is devolved from the lamentable situation where the normal age-related reduction in amplitude of accommodation reaches a point when the clarity of vision at near cannot be sustained for long enough to satisfy an individual's requirements" or according to Millodot, his Dictionary of Optometry and Visual Science defines presbyopia as "a refractive condition in which the accommodative ability of the eye is insufficient for near vision work, due to ageing".<sup>24-26</sup>

Some researches do not define presbyopia at all, but refer to its onset, which, as the decline in accommodation is well described to commence in the teenage years, implies a functional definition.<sup>27</sup>

Another approach to defining presbyopia has been to adopt a more physiological approach, describing presbyopia as an age-related progressive decline in the crystalline lens ability to accommodate, resulting in the inability to focus on near objects.<sup>28</sup>

While both objective and subjective measures of accommodation indicate that the accommodative response starts to decrease in the early age, there is only a concurrent drop in accommodative gain by the 5<sup>th</sup> decade, reducing near image quality and resulting in the apparent acceleration of symptoms in early presbyopia.<sup>29,30</sup>



Presbyopia has even been described as causing the loss of accommodation.<sup>31</sup>

Holden and colleagues identified two different definitions of presbyopia in epidemiological studies:

1. Functional presbyopia, defined as needing a significant optical correction added to the presenting distance refractive correction to achieve an absolute Jaeger (J) on the eye chart or relative near visual acuity (such as 1 line of acuity improvement) criteria.
2. Objective presbyopia, where the significant optical correction is defined (such as  $\geq 1.00D$ ) and added to the best optical distance correction to achieve a defined near visual acuity. In more recent epidemiological studies, however, presbyopia is typically defined as a person aged greater or equal to the age of 45 years who is unable to read binocularly J1 at 40 centimeters (cm) or at their habitual working distance, and additionally in some studies, limited to those whose near vision improves with additional lenses.<sup>32</sup>

The original Jaeger eye chart was developed in 1867 and contained seven paragraphs, each printed in a successively smaller font size. The smallest paragraph you could read when holding the chart approximately 40 centimeters away determined your near visual acuity.

Presbyopia is derived from Ancient Greek πρέσβυς” translated into Latin (présbus, “old man”) and ὄψ” (óps, “eye” or to “see like”).

Therefore, a functional definition to fit this etymology would be more appropriate; otherwise, a new term for the condition should be adopted like “readers diopter”. Perhaps a more apposite definition would be that presbyopia occurs when the physiologically normal age-related reduction in the eyes focusing range reaches a point, such that when optimally corrected for distance vision, the clarity of near vision is insufficient to satisfy an individual's requirements.<sup>33</sup>

## 1.4. NON-SURGICAL TREATMENT OF PRESBYOPIA

The goal of treatment is to compensate for the inability of the eyes to focus on nearby objects. Treatment options for presbyopia include: wearing corrective eyeglasses (including reading glasses) or contact lenses, undergoing refractive surgery, or placing lens implants for presbyopia.

### 1.4.1. EYEGLASSES

Eyeglasses are a simple, safe way to correct vision problems caused by presbyopia. Types of reading glasses include:

- a) Prescription reading glasses. Reading glasses are worn only when needed to see close objects and small print more clearly. If the patient does not have any other vision problems, he/she can use glasses with prescription lenses for reading only. They will need to remove these when they're not reading. Most prescription reading glasses range in power from +1.00D to +3.00D.
- b) Bifocals. Correct for near and far vision. Lenses of these glasses have a visible horizontal line that separates the patient's distance prescription above the line, and reading prescription below the line.
- c) Trifocals. These glasses have corrections for near, close-up work, intermediate distance vision (such as for computer screens), and distance vision. Trifocals come with two visible horizontal lines in the lenses.
- d) Progressive multifocals. This type of lens has no visible horizontal lines, but has multiple powers for distance, intermediate distance and close-up corrections. Different areas of the lens have different focusing strengths. Refraction changes gradually in the lens from top to bottom.
- e) Office progressives. These lenses have corrections for computer-distance and close-up work.

## 1.4.2. CONTACT LENSES

Some people prefer to wear contact lenses rather than eyeglasses. This option may not work if the patient has certain conditions related to their eyelids, tear ducts or the surfaces of their eyes such as dry eye.

There are two types of contact lenses that help presbyopia. Monovision and multifocal contact lenses are very common treatments for presbyopia.

- a) Monovision contacts. They offer different prescriptions for each eye; one for distance vision and one for near vision. On the dominant eye, eye that focus objects in the distance has full correction for achieving good distant vision but on the non-dominant eye has reading prescription. The brain learns to favor one eye or the other for different tasks.
- b) Multifocal contacts. Multifocal contact lenses function in a manner similar to bifocal eyeglasses and are designed to provide clear vision across various focal points. These lenses have several rings or zones set at different powers. With this design, patients are actually using both near and far vision at the same time. The brain learns to automatically select the correct focus for what the patient wants to see. The ophthalmologist finds the lenses that best fit the patient, whether it is a soft lens, a rigid gas permeable (RPG) lens, or a hybrid lens. Multifocal lenses are also available as disposable lenses.

## **1.5. SURGICAL TREATMENT OF PRESBYOPIA**

### **1.5.1. LENTICULAR APPROACHES**

Refractive lens exchange (RLE) is a surgical procedure that involves replacing the natural crystalline lens of the eye with an artificial lens alternative. Refractive lens exchange treatment for presbyopia is similar to that used for cataract surgery. An artificial intraocular lens (IOL) replacement can improve near vision and reduce a person's dependence on reading glasses.

#### **1.5.1.1. Implantation of multifocal intraocular lens**

Implantation of a multifocal intraocular lens (MFIOL), introduced more than 20 years ago, is a popular procedure that achieves good visual acuity for both distant and near vision.<sup>34,35</sup>

#### **1.5.1.2. Types of multifocal intraocular lens**

Generally speaking, there are 3 types of multifocal intraocular lens: refractive, diffractive, and a combination of diffractive and refractive.<sup>36,37</sup>

The ultimate goal of clear lens extraction is to replace the crystalline lens with an intraocular lens that simulates the original function of the crystalline lens and provides the patients with a full range of functional vision for all distances. Precise biometry, accurate intraocular lens power calculation, good surgical technique as well as patient selection are crucial in achieving the best visual outcome and patient satisfaction.

Multifocal IOLs can improve uncorrected near visual acuity (UNVA) and uncorrected distance visual acuity (UDVA). Nevertheless, different IOL models provide different levels of improvement for uncorrected intermediate visual acuity (UIVA).<sup>38</sup>

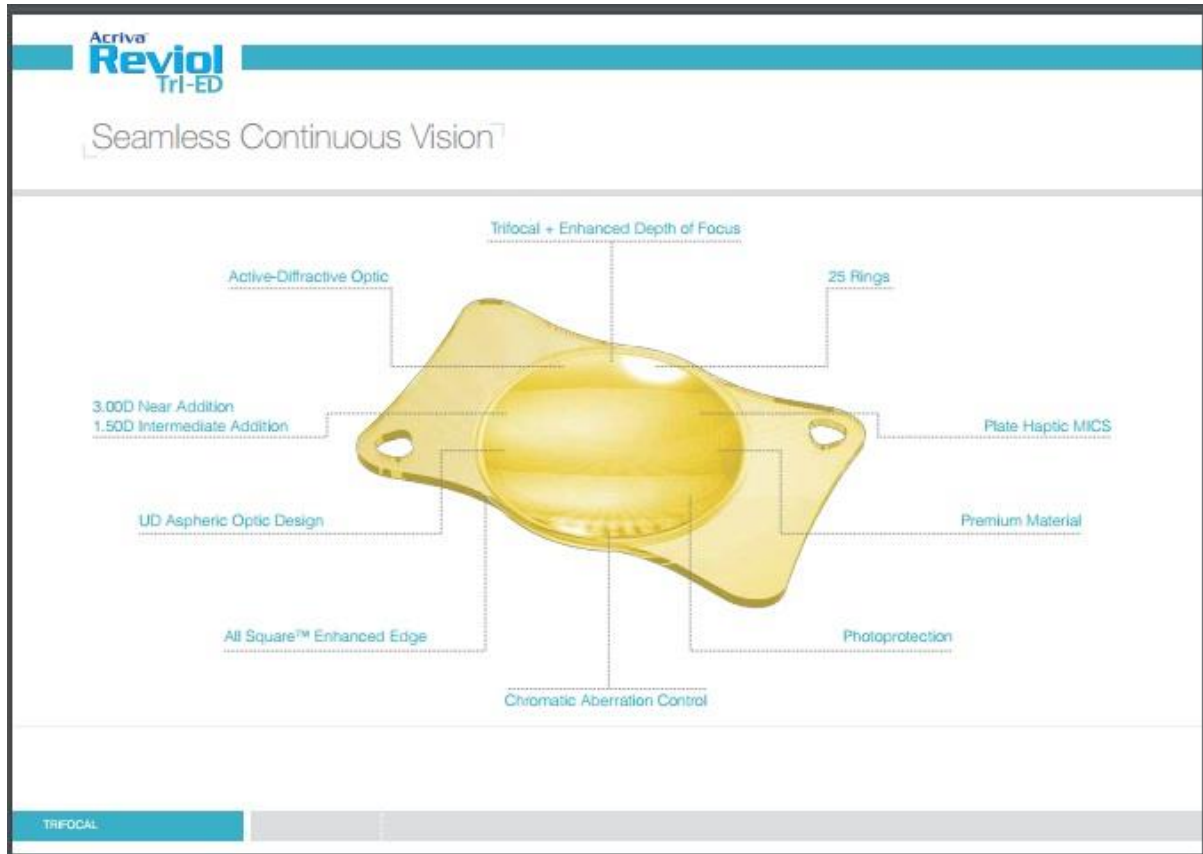
Multifocal IOLs with diffractive optic design, provide better near vision and reading performance than refractive multifocal IOLs and monofocal IOLs.<sup>39</sup>

### **1.5.1.3. Acriva Reviol Tri-ED**

The Acriva Reviol Tri-ED is a type of IOL that has a one-piece diffractive trifocal enhanced depth of focus (EDOF) design. The trifocal-EDOF combination is created by changing the height, width, interval, and number of the diffractive rings, with the entire optic diameter covered by 25 rings. There is a real trifocal structure at both the center and periphery, in contrast with other available trifocal IOLs.

The EDOF feature of the lens provides a different advantage from the other available trifocal IOLs. Its semi-apodised active diffractive trifocal structure is designed to reduce unwanted diffraction to increase optical quality with enhanced depth of focus vision. The entire optic diameter covers 25 diffractive rings. This IOL has a trifocal anterior surface and provides an addition of +3.00D for near vision and +1.50D for intermediate vision at the IOL plane. Its design allocates 44 percent (%) of light to distance, 28% to intermediate, and 28% to near for photopic and mesopic light condition; its overall efficiency of global light transmittance is 89.1%. The IOL is fully independent of pupil diameters and provides adequate visual performance under all lighting conditions. It has a plate-haptic design with no haptic angulation with an all enhanced 360 degree square edge to prevent posterior capsule opacification formation. It has spherical powers of 0.00D to 32.00D in 0.50D increments. The Reviol Tri-ED can be implanted with the single-use Acrijet Blue 1.8 mm injector (VSY Biotechnology) through a 2 mm incision.<sup>40,41</sup>

Figure 3. Tri-ED IOL



Courtesy of VSY Biotechnology

Table 1. General IOL parameters

<b>Parameters</b>	<b>Reviol Tri-ED 611</b>
<i>Material</i>	<i>Hydrophobic surface, acrylic with 25% water content, blue filter</i>
<i>Optic size</i>	<i>6.00 mm</i>
<i>Optic design</i>	<i>Active-Diffractive Tri-ED</i>
<i>Haptic size</i>	<i>11.00 mm</i>
<i>Haptic Design</i>	<i>Plate Haptic</i>
<i>Haptic Angle</i>	<i>0°</i>
<i>Recommended Ac. A Constant</i>	<i>118.0</i>
<i>Recommended Op. A Constant</i>	<i>Srk-T: 118.3 – SRK-II: 118.5</i>
<i>Diopter Power Range</i>	<i>From 0.0D to +32.00D (0.50D increments)</i>
<i>Refractive Index Dry</i>	<i>20 °C/35 °C 1.509/1.509 ± 0.002</i>
<i>Refractive Index Wet</i>	<i>20 °C/35 °C 1.462/1.462 ± 0.002</i>
<i>Light distribution (far%/intermediate%/near%)</i>	<i>44/28/28</i>
<i>Transmission Value (%)</i>	<i>89.1</i>
<i>Chromatic Aberration Control (Abbe number)</i>	<i>58</i>
<i>PCO prevention</i>	<i>360° sharp edge</i>
<i>Recommended Injector and Cartridge System</i>	<i>Acrijet</i>

## **1.5.2. CORNEAL APPROACHES**

The history of surgical presbyopia treatment has oscillated with numerous promising ideas that have fallen short of success. An early effort included the addition of human donor corneal tissue to a patient's host cornea to change the refraction, a procedure called additive refractive keratoplasty.<sup>42</sup>

In 1949, Jose Barraquer introduced the first corneal inlay prototype. Created for the treatment of high myopia or aphakia, it was designed from polymethylmethacrylate or flint glass. These early inlays showed initial signs of success in treating the targeted refractive error. However, the abhorrent rates of implant extrusion and corneal necrosis from reactions to the material quickly resulted in these inlays becoming unfavorable.<sup>43,44</sup>

Two decades after Barraquer experimented with his initial prototype, the concept was revived with the discovery of more biocompatible materials, like hydrogel.<sup>45</sup>

These new materials showed promise in that they were transparent and permeable to fluids and nutrients, which provided some assurance that the corneal tissue would tolerate them. Unfortunately, the majority of these devices were explanted because of the aggressive rates of stromal thinning, melting, haze, inlay decentration, and corneal opacification.<sup>46-49</sup>

### **1.5.2.1. Corneal inlays**

Corneal inlays represent presbyopia treatment that involve inserting a small plastic ring with a central opening into the cornea of one eye. The opening acts like a pinhole camera and allows in focused light so that close objects can be seen.

They are typically implanted into the cornea, at the front of the eye, during a minimally invasive surgical procedure, restoring close-up vision of the eye that is not dominant. Corneal inlay increases the depth of focus of the treated eye and reduces the need for reading glasses without significantly affecting the quality of distance vision. Corneal inlays are a reversible procedure.

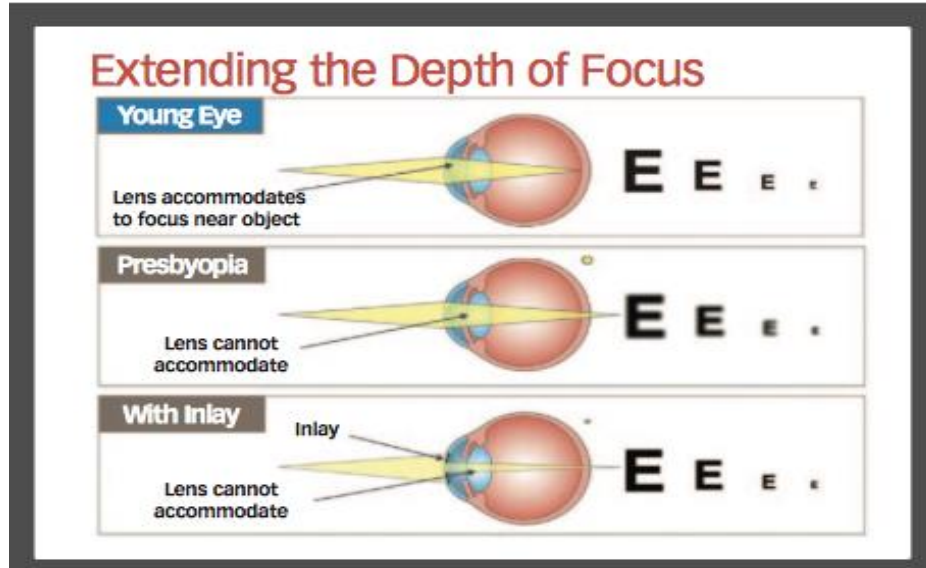


### 1.5.2.2. Types of corneal inlays

Currently, there are three available styles of corneal inlays:

- a) Flexivue Microlens™ (Presbia Coöperatief U.A., Irvine, CA, USA) - is a transparent, hydrogel-based, concave–convex disc composed of an optically clear copolymer of hydroxyethyl methacrylate and methyl methacrylate containing an ultraviolet blocker with a 3 mm diameter and 15-20 micrometers ( $\mu\text{m}$ ) thickness, depending on the additional power.<sup>50</sup>
  
- b) Raindrop® Near Vision Inlay (ReVision Optics, Lake Forest, CA, USA) – this inlay is a clear, permeable, positive meniscus-shaped biocompatible hydrogel implant that is designed to closely resemble the human cornea. It has a diameter of 2 mm, a center thickness of 32  $\mu\text{m}$  and approximately the same refractive index as the cornea. The Raindrop Inlay treats presbyopia in a manner similar to multifocal contact lenses by changing the curvature of the eye.
  
- c) KAMRA™ inlay (AcuFocus Inc., Irvine, CA, USA) – this corneal inlay is implanted in the non-dominant eye where its pinhole design allows it to extend the patient's range of vision from near to far. KAMRA inlay blocks unfocused light and narrows the macular blur circle, thereby extending depth of focus.<sup>51</sup>

Figure 4. KAMRA inlay extending depth of focus



*Courtesy of Dr Jay S Popose, MD*

### 1.5.3. CONDUCTIVE KERATOPLASTY (CK)

This procedure uses radiofrequency energy to apply heat to tiny spots around the cornea. The heat causes the edge of the cornea to shrink slightly, increasing its curve (steepness) and focusing ability. The results of conductive keratoplasty are variable and may not be long lasting. Treatment with CK is based on the effect of temperature on the biomechanical properties of the cornea.<sup>52</sup>

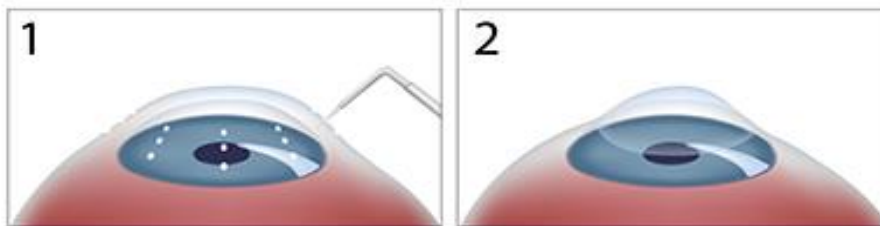
At 55-65° Celsius (C), collagen dehydrates and retracts, but retains its original configuration on cooling. At temperatures above 70-100°C, however, collagen completely denatures resulting in necrosis and permanent damage.

Conductive keratoplasty delivers a controlled-released radiofrequency current of 350-400 kilohertz (kHz) within the peripheral corneal stroma to a depth of 500 µm through a thin, handheld probe (keratoplasty tip; Refractec Inc., Irvine, California).

The electrical impedance to energy flow through the collagen fibrils increases the tissue temperature to the 65°C target resulting in controlled shrinkage of the peripheral collagen lamellae.<sup>53</sup>

Circles of eight spots are created by repeated insertion of the probe at 6, 7 or 8 mm circumference optical zones as determined by nomogram for a total of 8, 16, 24, or 32 spots. Shrinking the peripheral collagen has a tightening effect on the mid-peripheral cornea, which causes an increased curvature of the central cornea, thereby increasing refractive power.

Figure 5. Conductive keratoplasty



## Conductive Keratoplasty (NearVision CK)

Courtesy of  Clínica de  
Oftalmología  
de Cuiú S.A.

## 1.5.4 REFRACTIVE SURGERY

The general demand for spectacle independence has been growing strongly in recent times, and has made the correction of presbyopia one of the most important and last frontiers of refractive surgery.

### 1.5.4.1. Laser in situ keratomileusis

The term keratomileusis originates from the Greek words for “cornea” (kerato) and “to carve” (mileusis). Laser in situ keratomileusis (LASIK), 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.

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 a 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 -10.00D to +6.00D, and up to  $\pm 6.00D$  cylinders of astigmatism.<sup>54-56</sup>

The flap, which averages in thickness from 90 to 130 microns, 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 within several minutes. Patients are instructed not to rub or squeeze their eyes.<sup>57-62</sup>

Although LASIK cannot treat the root cause of presbyopia, there are LASIK variations that can help reduce the patient’s need for reading glasses. Refractive surgery changes the shape of cornea. For presbyopia, this treatment can be used to improve close-up vision in non-dominant eye.

## 1.5.5. EXCIMER LASERS

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.<sup>63,64</sup>

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 nanometer (nm). This wavelength falls in the ultraviolet short wave (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.<sup>65,66</sup>

Laser energy at 193 nm is very well absorbed by the proteins, glycosaminoglycans and nucleic acids comprising the cornea. Since 193 nm photons is of higher energy than the molecular bond strength of these compounds, absorption of the laser energy results in breaking of the bonds. The resulting molecular fragments are ejected from the surface of the cornea at supersonic speeds.<sup>67,68</sup>

### 1.5.5.1. 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 lasers enable faster treatment (for given frequency) and are less sensitive for decentration, but they homogenize slower, give irregular treatment of the surface and have a 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.<sup>69</sup>

Newer generation 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 exceeded some limitations of full beam systems, but maintained the speed of the treatment and low decentration sensitivity. The system uses an additional diaphragm between the 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.

Flying spot systems convert the laser beam into a small round spot (between 0.6 and 2.0 mm). The system uses only the central, most homogenic part of the beam, and beam direction is controlled by a mirror with rotation function. Ablation of the targeted tissue is performed by repeated delivery of a 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, the 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. The energy profile of every spot is Gaussian and enables smooth areas of ablation, and the distance between two aiming spots is half of one beam size so that the regular ablation can be provided. The main advantage of these systems is the possibility of treatment for high levels of irregularities. The smaller the spot, the treatment option of irregularities is higher.<sup>69</sup>

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-Width-at-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-Free™”) ablation algorithm is designed to maintain the preoperative levels of ocular higher-order aberrations.<sup>70-73</sup>

Aspheric aberration neutral (Aberration-Free™) profiles are not based on the Munnerlyn proposed profiles, and go beyond that by adding some aspheric characteristics to balance the induction of spherical aberration (prolateness optimization).<sup>74-76</sup> The profile is aspherical-based, including a multi dynamic 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 are 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 of  $>400$  millijoule/square centimeter ( $\text{mJ}/\text{cm}^2$ ), 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 ( $<200$   $\text{mJ}/\text{cm}^2$ ), aimed to reduce the amount ablated per pulse and to 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.

Figure 6. Schwind Amaris 750S laser platform



Courtesy of Schwind platform

### 1.5.6. MICROKERATOMES

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 intraocular pressure (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.<sup>77</sup>

Last generations of microkeratomes allow very precise flap creation with regular edges and predetermined thickness and shape. The procedure lasts only a 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 divided according to the movement of the dissection head. Nowadays, frequently used microkeratomes use linear, arcuate or pendular movement.

1. Linear movement (translation) – the dissecting head is led over two parallel tracks in a horizontal plane. Linear microkeratomes have the ability to create only nasal hinge.
2. Arcuate movement (translation) – the dissecting head is led in the horizontal plane over the eccentric axis circular track. Arcuate microkeratome has multiple options for hinge position.



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

Microkeratomers are made for single and multi-use purposes

Majority of microkeratomers are reusable after disassembling, cleaning and sterilization. The 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 2. Display of basic characteristics of commercially available microkeratomes

MANUFACTURER	MODEL OF MICRO KERATOME	TYPE OF MOVEMENT	FLAP THICKNESS	STANDARD DEVIATION (µm)	FLAP SIZE (mm)	HINGE POSITION
ZIEMER	Amadeus II	Linear	140-160-200-250-300-350-400-450	Not available	8.5-10	Superior/nasal
MORIA	M2 single use 90 SBK One Use + 90	Arcuate Linear	110-130-100	±15 ±8	8-11 8.8- 10.5	Superior Nasal
MED Logics	ML 7	Linear	100-130	±9	7.5-10	360° - possibility of choosing the position
SCHWIND	Carriazo-Pendular	Pendular	90-110-130-150-170	±10-12	9-10	360° - possibility of choosing the position
<p>Data about characteristics and performance of microkeratomes available at manufacturers links</p>						

## 1.6. MONOVISION LASIK

Monovision LASIK (monovision with an excimer laser) is a well-established technique that corrects one eye for distance vision (usually dominant eye) and the other eye for near vision, resulting in intentional anisometropia.<sup>78</sup>

The aim is to give functional near and distant visual acuity without the need for glasses. The mechanism that enables monovision to succeed is interocular blur suppression. Studies have reported success rates ranging from 80-98% for monovision post laser vision correction (LVC).<sup>79-82</sup>

The dominant eye is treated for distance vision to almost plano and the non-dominant eye is corrected to be slightly myopic for near vision up to -1.50D.

The mildly nearsighted eye is able to see things up close without reading glasses. The only problem is that distant vision with monovision LASIK is often not as crisp as it would be without the nearsightedness. Many people find this to be an acceptable tradeoff for improved near vision and, as such, monovision LASIK is the most widely used surgical correction for presbyopia.

Numerous accommodative and pseudo-accommodative approaches to treat presbyopia surgically exist. Each has its own benefits and limitations, and may involve some degree of compromise between the distance and near visual acuities. Accommodative approaches attempt to restore the true, dynamic and continuous range of the defocusing ability of the eye. Pseudo-accommodative approaches provide functional near vision from a variety of non-accommodative factors.

## **2. HYPOTHESIS**

Preoperative refractive error and patient age are factors that determine the appropriate choice between the two surgical procedures, lens surgery and Laser in situ keratomileusis.

### **3. AIMS OF THE RESEARCH**

1. To evaluate the effectiveness of two surgical methods for presbyopia treatment.
2. To investigate the differences in uncorrected near visual acuity (UNVA) in patients treated with two different surgical procedures.
3. To investigate the differences in uncorrected distant visual acuity (UDVA) in patients treated with two different surgical procedures.
4. To investigate the differences in residual refractive error in patients treated with two different surgical procedures and their effect on presbyopia.
5. To establish the protocol of patient selection for one of two surgery procedures.
6. To compare the overall outcome in visual performances between two surgical procedures.
7. To compare the overall patient satisfaction rate with both surgical methods.

## **4. PATIENTS AND METHODS**

### **4.1. PREOPERATIVE EXAMINATION**

The research was performed at the University Eye Hospital "Svjetlost" in Zagreb, Croatia. Patients were included during time period between January 2015 and December 2015 with a follow up of six months. During the inclusion period, 1020 patients, aged 45-55 years old were examined for refractive surgical procedures (LASIK or refractive lens exchange) at the Cornea and Refractive Surgery Department.

The inclusion criteria were: patients aged 45-55 years with a refractive error for myopic patients with  $\geq -3.00D$  of spherical equivalent (SE), for hypermetropia patients with SE of  $\geq +1.00D$ , astigmatism less than  $1.00D$ , and unremarkable corneal topography, as well as no signs of cataract and no other ocular or systemic diseases. Patients with peripheral retinal degeneration were evaluated by a retina specialist and subjected to argon photocoagulation before the refractive procedure when indicated.

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

Out of 1020 patients, 360 patients were not suitable for any of the surgical procedures because of their high refractive error and/or inadequate ratio of refractive error. Most of the excluded patients were plano presbyopia or combination of myopia or hypermetropia exceeding inclusion criteria. Other had irregularities of the cornea and/or ectatic corneal disease (60 patients), retinal problems (45 patients), amblyopia less than 0.5 visual acuity (55 patients), previous eye injuries (31 patients), newly discovered glaucoma (25 patients) and alternative ocular diseases such as acquired or congenital cataract (40 patients).

Two hundred and thirty-one patients who met all the criteria were included in the study. Out of 231 operated patients, 198 patients (396 eyes) completed the six months of study follow-up.

Initially 200 patients were planned for the study, so that found data of the research was valid (up to 15% loss of patients is considered allowable for needed data of this research). The study followed patients that underwent either refractive lens exchange (RLE) with multifocal intraocular lens implantation (MFIOL group) or Laser in Situ Keratomileusis procedure on cornea (LASIK group) and subsequently analyzed the refractive data and visual performances and their satisfaction rate. Within each group, we further analyzed the treated eyes according to the type of diopter: myopic or hypermetropia patients. A total of 200 eyes (100 patients) were included in the MFIOL group. There were 110 eyes (55 patients) with hypermetropia and 90 eyes (45 patients) with myopia who underwent lens surgery. A total of 198 eyes (99 patients) were included in the LASIK group, 100 eyes (50 patients) with hypermetropia and 98 eyes (49 patients) with myopia.

## **4.2. METHODS**

### **4.2.1. PREOPERATIVE EXAMINATION**

Every patient underwent complete preoperative ophthalmologic examination prior to deciding if the patient met the criteria for the surgery. Examination included uncorrected and best corrected distant visual acuity (UCDVA, BCDVA), uncorrected and best corrected near visual acuity (UCNVA, BCNVA), manifest and cycloplegic refraction, spherical equivalent (SE), corneal topography measured on pentacam (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany), aberometry (L 80 wave+, Luneau SAS, Prunay-le Gillon, France), tonometry (Auto Non-Contact Tonometer, Reichert Inc., Buffalo, NY, USA), slit-lamp and dilated funduscopy examination and patient satisfaction questionnaire. Visual acuity was measured using a standard Snellen acuity chart at 6 m and presented in a decimal format.<sup>83</sup> Near visual acuity was tested with Jaeger charts, reading on 30-40 cm distance. Patients with stable refraction for 1 year, with SE for hyperopic patients  $\geq +1.00D$ , and  $\geq -3.00D$  for myopic patients, and astigmatisms  $\leq 1.00D$ , were included. Ocular criteria were those normally adopted in refractive surgery either for refractive lens exchange or cornea surgery. Patients with a history of ocular surgery, abnormal corneal topography, and other ocular diseases 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 Sloan's letters was used.<sup>83,84</sup> 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. 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.<sup>84</sup> 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 a maximum of two letters was recorded (entered); in the case where there was larger number of misread letters, visual acuity of the 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.

The measurement of near visual acuity is dependent on a number of factors, such as distance visual acuity, accommodation capability, and near vision correction.<sup>83-84</sup> Because accommodation accuracy is dependent on viewing distance, it is important to adopt a fixed viewing distance during near vision assessments.

The American Academy of Ophthalmology underlines the importance and clinical relevance of near vision testing. Near vision testing is indicated for patients that come to the clinic for refractive surgery evaluation, or routine examination involving refraction, particularly for individuals aged 40 years and above, as well as for patients with symptoms at near vision such as blurred vision or discomfort. Uncorrected and corrected near visual acuity were measured with standardized Jaeger charts.<sup>85</sup>

The American Academy of Ophthalmology prescribes that near vision should be measured at 14 to 16 inches (35-40 cm) or at the patient's preferred reading distance. Ideally, the patient is tested under corrected and uncorrected circumstances at an appropriate distance as determined by the patient's needs. The viewing distance recommended is 40 cm for easy comparison between near and distance visual acuity, because at this distance, the influence of accommodation is minimal.<sup>86</sup>

### **4.3. PATIENTS SATISFACTION QUESTIONNAIRE**

Reporting patient satisfaction has become an increasingly common component of studies evaluating treatment outcomes. Often, patient satisfaction is more subjective and determined by a qualitative comparison of the vision experienced postoperatively, balanced with their preoperative expectations. As the predictability of refractive correction and visual outcomes improve, patient satisfaction and managing patient expectations become key in the context of modern ophthalmology.<sup>87</sup> Simply correcting the refractive error is no longer the only consideration, and patients, particularly those within the working-age population, expect that the procedure will positively influence their quality of life. Patients were tested by patient satisfaction questionnaire developed at the Eye Clinic Svjetlost for all patients that undergo refractive surgery in order to improve their satisfaction and expectations. The questionnaires were completed preoperatively, and one month, three months and six months postoperatively. It had 5 possible responses, that are rated from 1-5.

The ranging was following:

1. not satisfied at all,
2. a little bit,
3. a moderate amount,
4. a lot,
5. very satisfied.

## **4.4. SURGICAL TECHNIQUE**

### **4.4.1. REFRACTIVE LENS EXCHANGE WITH MULTIFOCAL INTRAOCULAR LENS IMPLANTATION**

Prior to the surgery, two drops of topical anesthetic (Novesine, OmniVision GmbH, Puchheim, Germany) were instilled at 2 minutes intervals. The IOLMaster 500 (Carl Zeiss Meditec, Jena, Germany) was used for preoperative biometry and IOL power calculations. Proper sterile precautions were taken to prepare the area for surgery, including use of antiseptics such as povidone-iodide. Sterile drapes, gowns and gloves are employed. A plastic sheet with a receptacle helps collect the fluids during phacoemulsification. When the patient was positioned on the operative table, the eye to be treated was cleaned with 2.5% povidone iodide. After topical anesthesia and adequate dilation, a lid speculum is used to hold the eyelids apart. First, the procedure was performed on the right eye. When it was completed, the same procedure was repeated on the left eye. An eye speculum was inserted to keep the eyelids open.

Phacoemulsification was performed using an Infinity phacoemulsification machine (Abbott Medical Optics White Star Signature Phacoemulsification System). Most phacoemulsification machines have parameters for power, vacuum, pulse, burst, and oscillation levels, as well as bottle height. These may be set to allow certain phaco procedures to proceed during different steps of phacoemulsification surgery.

All surgeries were performed by the same experienced surgeon using a standard technique of sutureless micro coaxial 1.8-2.2 mm phacoemulsification. All incisions were made at the steep axis of the cornea. A 1.8 mm incision was made and 1.8 mm injector was used. In case of difficulty, the incision was extended up to 2.2 mm. After capsulorhexis creation and phacoemulsification, the IOLs were inserted into the capsular bag using the Acrijet Blue injector (VSY Biotechnology, Amsterdam, Netherlands) through the main incision. The foldable multifocal IOL was inserted and rotated into the intact capsular bag. The viscoelastic material was completely removed by irrigation and aspiration. All incisions were left sutureless. Postoperatively, all patients received the same treatment: a combination of an antibiotic and steroid agent.

Therapy included combination of topical antibiotic and steroid drops (Tobradex, Alcon, FortWorth, TX, USA) 5 times daily for 1 month, reducing the amount of drops every week, and artificial tears (Blink, Abbott Medical Optics, Santa Ana, CA, USA) 6-8 times daily for at least 1 month. Firstly, the procedure was performed on the right eye. When it was completed, the same procedure was repeated on the left eye. In refractive surgery, the goal is to achieve optimal visual acuity, optimal refraction (usually emmetropia), and no complications.

#### **4.4.2. LASER IN SITU KERATOMILEUSIS LASIK**

Prior to the surgery, two drops of topical anesthetic (Novesine, OmniVision GmbH, Puchheim, Germany) were instilled at 2 minutes 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. Firstly, 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 keratometry values), and then vacuum was applied. When adequate vacuum of 150 mm was accomplished, microkeratome motor with previously assembled 90  $\mu\text{m}$  blade was placed on the ring.

Blade of 90  $\mu\text{m}$  is predicted for creation of 110  $\mu\text{m}$  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 12 o'clock position on the superior conjunctiva. Corneal stroma was dried from the excess liquid with a triangle micro sponge, and excimer laser ablation was applied.

Schwind Amaris 750S (Schwind eye-tech-solutions, Kleinostheim, Germany) was used for the excimer laser treatment. 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 ( $>400 \text{ mJ/cm}^2$ ) 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 ( $<200 \text{ mJ/cm}^2$ ), aimed to reduce the amount ablated per pulse and smooth out the ablated stromal bed.

The mean optical zone of the treatment was  $6.63 \pm 0.20$  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  $8.67 \pm 0.31$  mm (range 7.9 to 9.0 mm). The Aberration Free™ program was applied in all cases. All ablations were centered on corneal vertex. The corneal vertex is the intersection of the pupillary axis with the anterior surface of the cornea, when the pupillary axis coincides with the optical axis of the measuring device.<sup>86</sup>

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, calculated by using the videokeratoscope (CSO, Costruzione Strumenti Oftalmici, Florence, Italy). The Cartesian coordinates of the corneal vertex were manually entered into the software program.<sup>86-87</sup>

For all patients, the programmed treatment consisted of cycloplegic spherical correction with manifest astigmatic power and axis. For this platform the sphere, cylinder, and axis were entered into laser without nomogram adjustment.<sup>88</sup>

Schwind Amaris 750S features a six-dimensional 1050Hz 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, especially 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 was instilled into the eye, and the eyelid speculum and sterile drape were gently removed.

#### **4.5. POSTOPERATIVE THERAPY**

Postoperative therapy for both MFIOL and LASIK patients 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.

## **4.6. POSTOPERATIVE EVALUATION**

All patients were examined 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month, 3<sup>rd</sup> month, and 6<sup>th</sup> month after the surgery. Evaluation included measurement of: uncorrected distance visual acuity, best corrected distance visual acuity, uncorrected near visual acuity, best corrected near visual acuity, manifest refraction, slit-lamp examination, tonometry, and corneal topography and patient satisfaction questionnaire.

## **4.7. STATISTICAL ANALYSIS**

Statistical processing and graphical presentation of the results were carried out using the software MS Excel 2016 (Microsoft, USA) and Statistics version 10.0 (Stat Soft Inc., Tulsa, OK, USA). The data obtained are presented as the average and SD ( $M \pm SD$ ). For comparison of two independent groups, Student's unpaired t-criterion was applied, and for comparison of dependent ones, the Student's t-test was applied. The critical level of significance of the null statistical hypothesis in accordance with the criteria accepted in biomedical research was taken as 0.05.

## **4.8. 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 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, presbyopia treatments.

## 5. RESULTS

### 5.1. REFRACTIVE LENS EXCHANGE WITH MULTIFOCAL IOLS (MFIOL GROUP)

A total of 200 eyes (100 patients) were included in the MFIOL group. There were 110 eyes (55 patients) with hypermetropia and 90 eyes (45 patients) with myopia who underwent lens surgery. The average age of the group was  $52 \pm 2.56$  years old, 61% female, 39% male, and all Caucasian. Patients were followed up for 6 months on time points: 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month, 3<sup>rd</sup> month and finally 6<sup>th</sup> month when manifested refraction in spherical equivalent, uncorrected near visual acuity, uncorrected distant visual acuity, best corrected near visual acuity and best corrected distant visual acuity were analyzed and statistically compared. Satisfaction questionnaire was given preoperatively and on 1<sup>st</sup> month, 3<sup>rd</sup> month and finally 6<sup>th</sup> month, respectively.

#### 5.1.1. MANIFESTED REFRACTION SPHERICAL EQUIVALENT

Preoperatively, mean spherical equivalent was for hyperopes  $1.81 \pm 0.8$  (min 1, max 4.5) and for myopes  $-5.41 \pm 1.39$  (min -3.25, max -9.00) D, while overall SE was  $-1.46 \pm 3.05$  (min -9.00, max 4.50) D. Six months postoperatively mean SE for hyperopes was  $0.38 \pm 0.79$  (min 0.75, max 1.25) and myopes  $0.32 \pm 0.65$  (min -2.00, max 1.25) D, which was statistically significant as compared to preoperative values in both groups ( $p < 0.05$ ). As expected, there was no statistically significant differences between hyperopes and myopes in manifest refraction after 6 months ( $p = 0.46$ ).

Mean hyperopic group SE in other following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were  $0.40 \pm 0.80$ D,  $0.40 \pm 0.80$ D,  $0.39 \pm 0.80$ D and  $0.39 \pm 0.75$ D, respectively, which were all statistically significant as compared to preoperative values ( $p < 0.05$ ).

Mean myopic group SE in all following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were  $0.34 \pm 0.50$ D,  $0.34 \pm 0.50$ D,  $0.33 \pm 0.50$ D and  $0.35 \pm 0.60$ D, respectively, which were all statistically significant as compared to preoperative values ( $p < 0.05$ ).



Table 3. Manifested refraction (spherical equivalent (diopters) comparison between hyperopes and myopes, SDEV (standard deviation).

	Manifested refraction SE (diopters/mean±SDEV(min-max))	
	preop	6 months
<b>Hyperopes</b>	1.82±0.79 (1-4.5)	0.38±0.79 (0.75-1.25)
<b>Myopes</b>	-5.41±1.38 (9.0- -3.25)	0.32±0.65 (1.25- -2.00)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistical significant</b>	*p= 6.82E-31	p=0.46

Figure 7. Manifested refraction in hyperopes preoperatively (preop) and 6 months postoperatively (postop). SE (spherical equivalent), D (diopters).

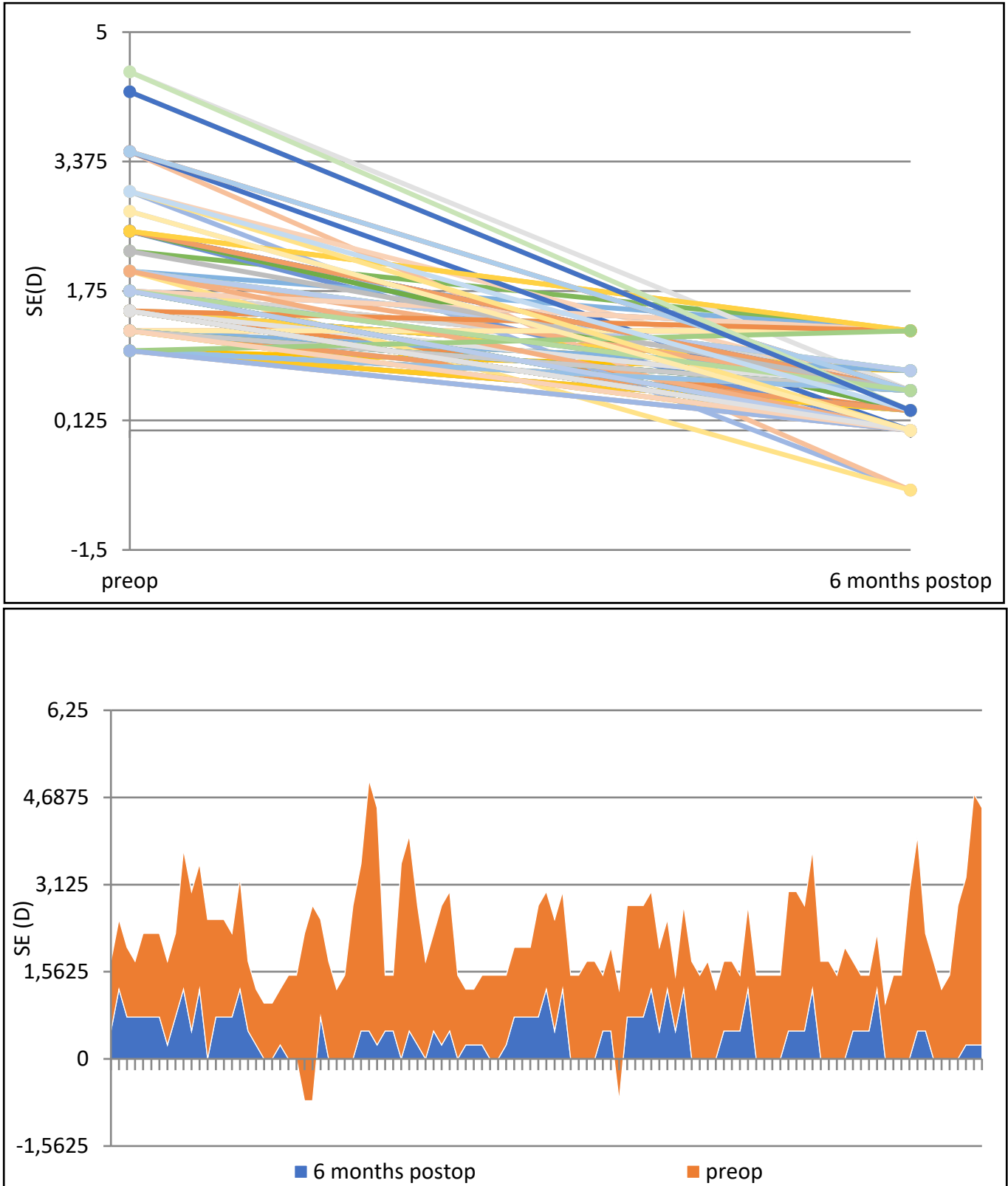
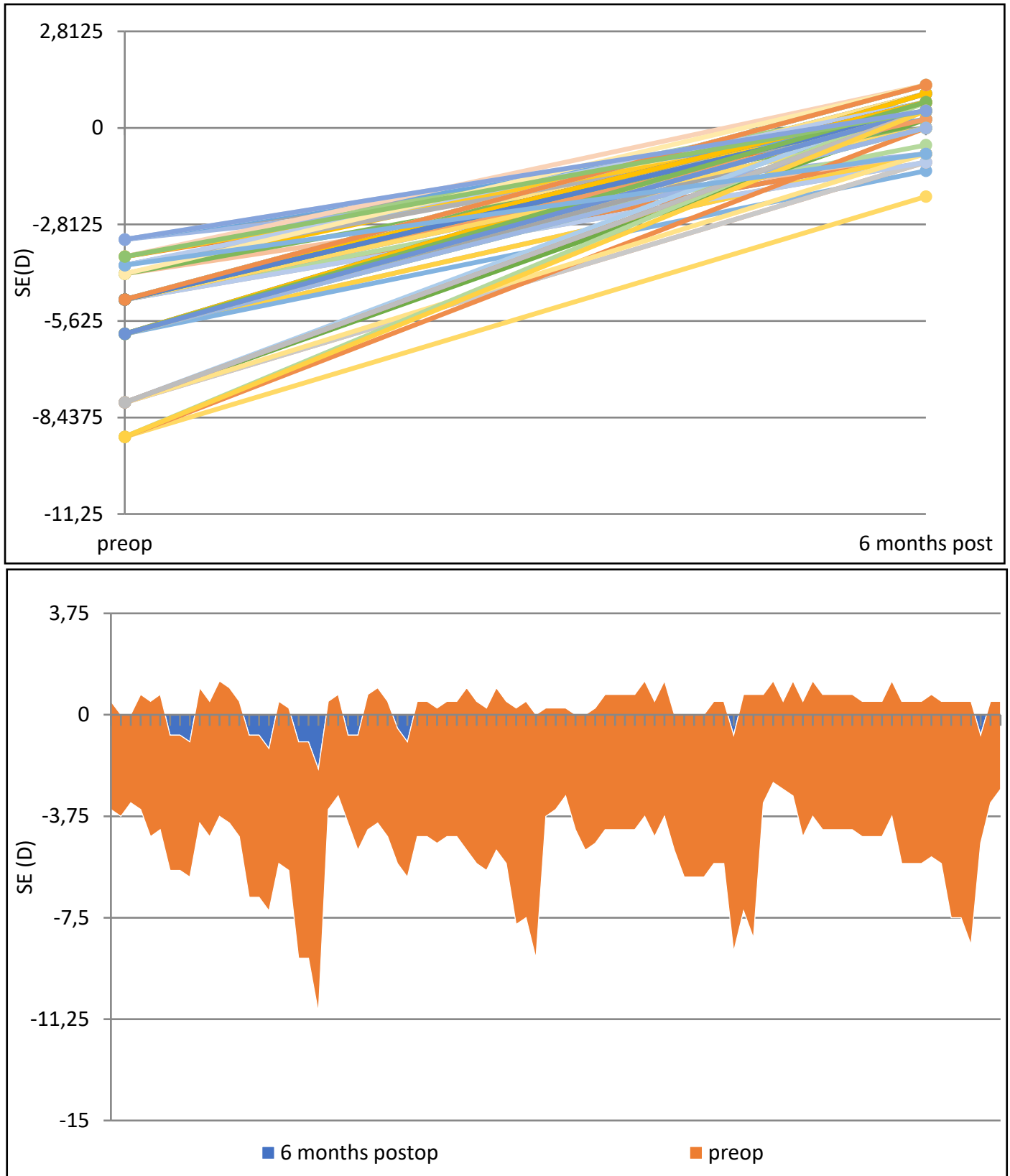


Figure 8. Manifested refraction in myopes preoperatively (preop) and 6 months postoperatively (postop). SE (spherical equivalent), D (diopters).



### **5.1.2. UNCORRECTED AND BEST CORRECTED NEAR VISUAL ACUITY**

Mean preoperative UCNVA was in hyperopes  $4.22 \pm 0.88J$  (min 2, max 5) while in myopes  $2.54 \pm 0.79J$  (min 1, max 4). Overall, UCNVA was  $3.45 \pm 0.99J$  (min 1, max 5). Six months postoperatively, UCNVA was  $1.16 \pm 0.37J$  (min1, max 2) in hypermetropic eyes and  $1.43 \pm 0.47J$  (min1, max 3) in myopic eyes, respectively, which was statistically significant as compared to preoperative values in both groups (student t-test,  $p=7.48E-30$ ,  $p=6.89E-25$ ).

However, there was also statistical significance between hyperopes and myopes at six months point ( $p=2.88E-05$ ).

Mean hyperopic group UCNVA in other following points 1<sup>st</sup> day, 1<sup>st</sup> month and 3<sup>rd</sup> month were  $1.40 \pm 0.80J$ ,  $1.39 \pm 0.70J$  and  $1.20 \pm 0.75J$ , respectively, which were all statistically significant as compared to preoperative values ( $p < 0.05$ ).

Mean myopic group SE in all following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were  $2.14 \pm 0.50J$ ,  $2.11 \pm 0.50J$ ,  $1.84 \pm 0.25J$  and  $1.55 \pm 0.60J$ , respectively, which were all statistically significant as compared to preoperative values ( $p < 0.05$ ).

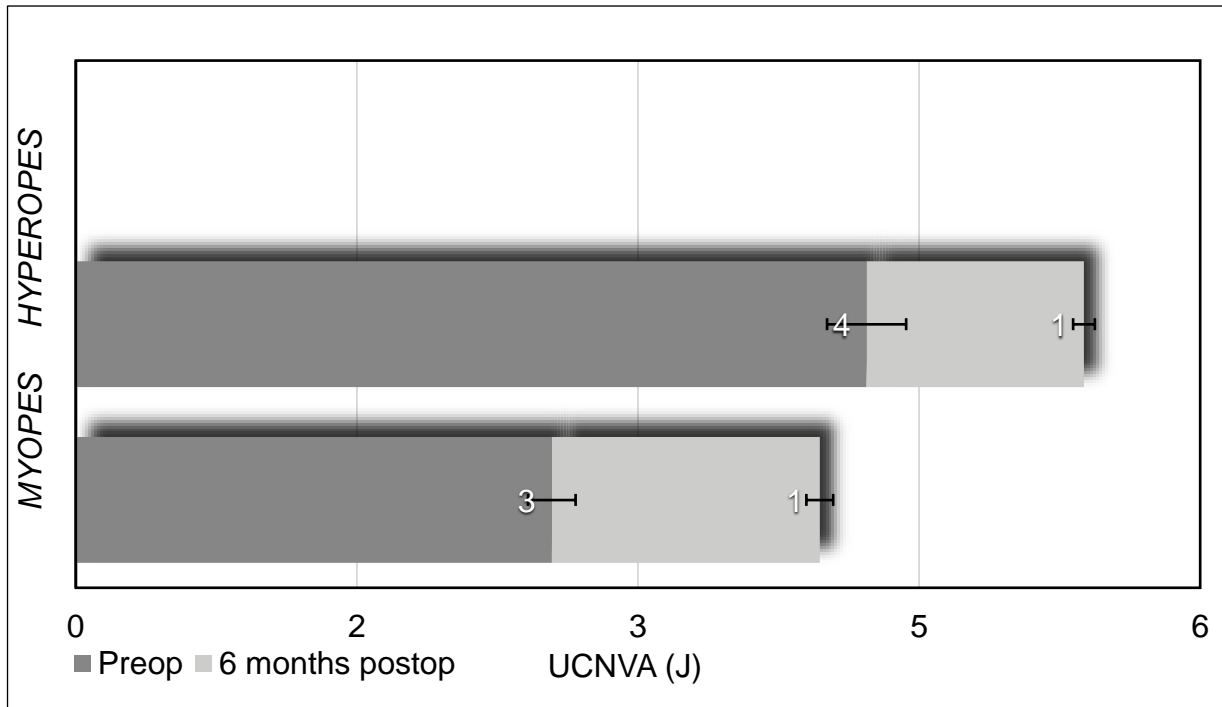
Mean preoperative best corrected near visual acuity was  $1.01 \pm 0.01J$  (min 1, max 1.5) in hyperopes, while in myopes it was  $1.03 \pm 0.19J$  (min 1, max 2).

Overall preoperative BCNVA in MFIOL group was  $1.02 \pm 0.15J$  (min 1, max 2). Six months postoperative BCNVA in hypermetropic eyes was  $1.01 \pm 0.03J$  (min 1, max 1.5) and in myopic eyes  $1.05 \pm 0.20J$  (min 1, max 2), which was not statistically different as compared to preoperative values nor in comparison of groups. The similar trend was seen in all other time points.

Table 4. Uncorrected near visual acuity UCNVA (J) comparison between hyperopes and myopes. J (Jaegers).

	UCNVA (Jaeger/mean±SDEV(min-max))	
	preop	6 months
<b>Hyperopes</b>	4.22±0.88 (2-5)	1.16±0.37 (1-2)
<b>Myopes</b>	2.54±0.4779 (1-4)	1.43±0.47 (1-3)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistical significant</b>	*p= 7.52E-32	*p=2.88E-05

Figure 9. UCNVA (J) comparison between hyperopes and myopes preoperatively (preop) and 6 months postoperatively (postop). UCNVA (Uncorrected near visual acuity), J (Jaegers).



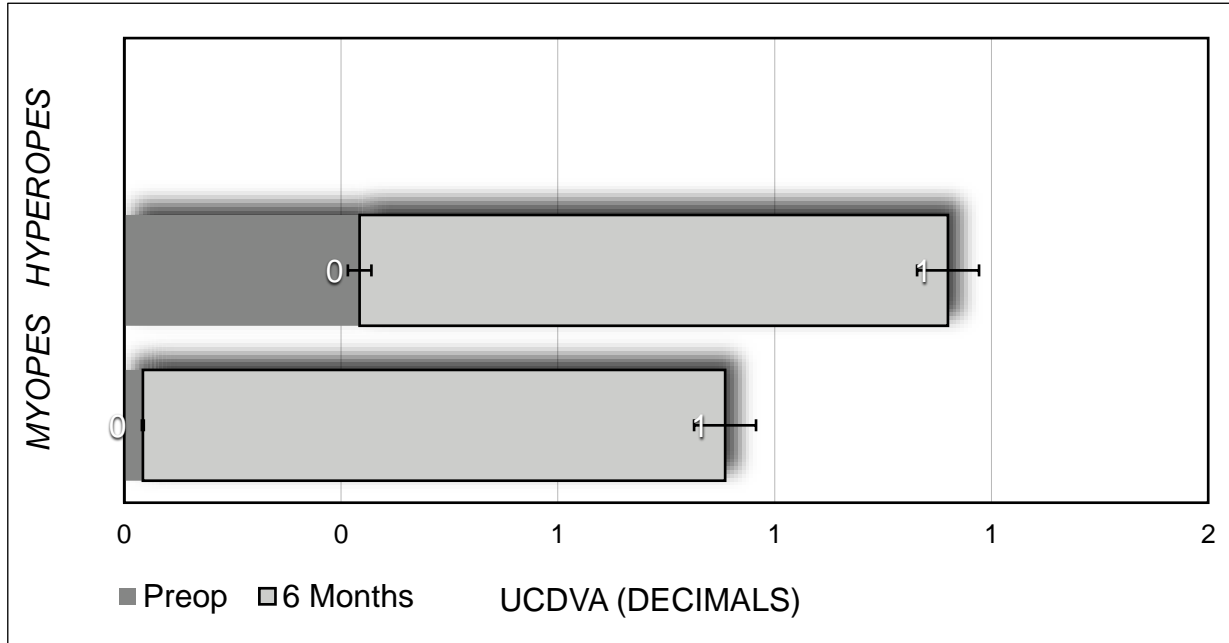
### 5.1.3. UNCORRECTED AND BEST CORRECTED DISTANT VISUAL ACUITY

Mean preoperative uncorrected distant visual acuity (UCDVA) (decimals) was  $0.39 \pm 0.24$  in hyperopes (min 0.05, max 1.0), while in myopes it was  $0.04 \pm 0.02$  (min 0.01, max 0.05). Overall, UCDVA was  $0.23 \pm 0.24$  (min 0.01, max 1). Six months postoperatively, UCDVA was  $0.95 \pm 0.07$  (min 0.65, max 1) in hypermetropic eyes and  $0.94 \pm 0.08$  (min 0.65, max 1) in myopic eyes, respectively, which was statistically significant as compared to preoperative values in both groups (student t-test,  $p=9.45E-30$ ,  $p=7.88E-36$ ). There was no statistical significance between hyperopes and myopes at the six months point ( $p=0.43$ , Table 5, Chart 4).

Table 5. Uncorrected distant visual acuity comparison between hyperopes and myopes. SDEV (standard deviation).

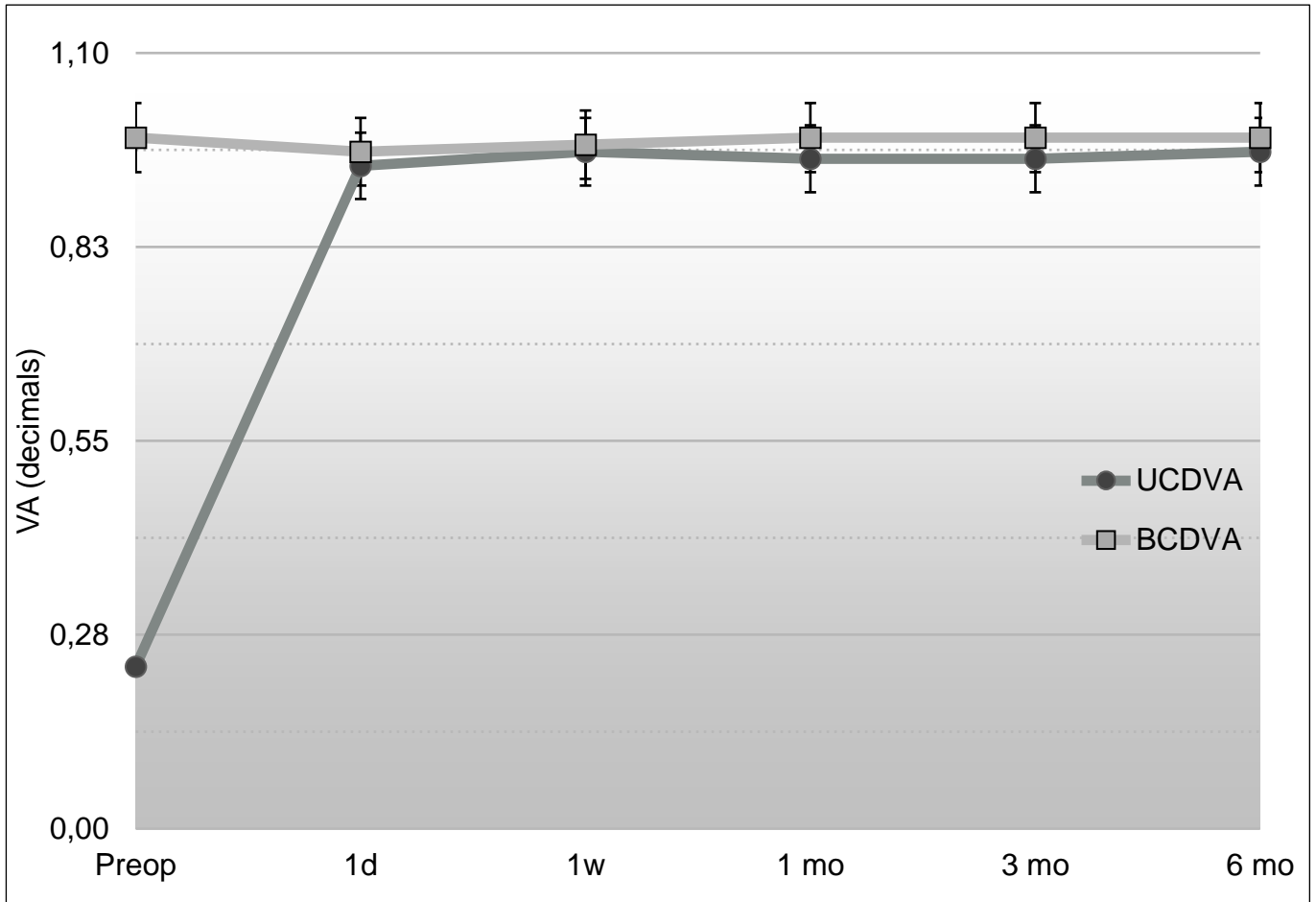
	UCDVA (decimals/mean+/-SDEV(min-max))	
	Preop	6 months
<b>Hyperopes</b>	$0.39 \pm 0.24$ (0.05-1)	$0.95 \pm 0.07$ (0.65-1)
<b>Myopes</b>	$0.04 \pm 0.02$ (0.01-0.05)	$0.94 \pm 0.08$ (0.65-1)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistical significant</b>	*p= 2.74E-29	p=0.43

Figure 10. UCDVA (decimals) comparison between hyperopes and myopes preoperatively (preop) and 6 months postoperatively (postop). UCDVA (Uncorrected near visual acuity).



Mean preoperative best corrected near visual acuity (BCDVA) was  $0.98 \pm 0.03$  in hyperopes (min 0.95, max 1.0) while in myopes it was  $0.96 \pm 0.05$  (min 0.95, max 1). Overall, preoperative BCDVA in MFIOL group was  $0.98 \pm 0.05$  (min 0.95, max 1). Six months postoperative, BCDVA in hypermetropic eyes was  $0.99 \pm 0.01$  (min 0.95, max 1.0) and in myopes  $0.97 \pm 0.03$  (min 0.95, max 1) which was not statistically different as compared to preoperative values nor in comparison of groups. The similar trend was observed in all other time points.

Figure 11. UCDVA and BCDVA (decimals) throughout time (follow up 6 months). UCDVA (uncorrected distant visual acuity), BCDVA (best corrected distant visual acuity), VA (visual acuity), d (day), w (week), mo (month).





### 5.1.4. PATIENTS SATISFACTION

Satisfaction questionnaire was given preoperatively and postoperatively on 1<sup>st</sup> month, 3<sup>rd</sup> month and 6<sup>th</sup> month, respectively. The score of patient satisfaction was from 1-5, where score 1 mean not satisfied, and score 5 mean very satisfied.

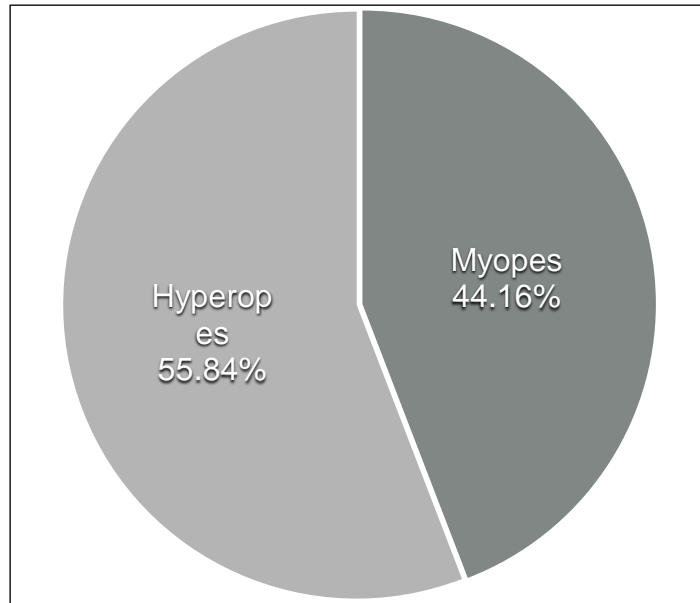
Preoperatively mean results in hypermetropic eyes group were  $2.03 \pm 0.51$ , while in myopic eyes were  $2.08 \pm 0.66$ . On 1<sup>st</sup> month, hyperopes were significantly satisfied, as the score was  $4.78 \pm 0.32$  ( $p=0.00009$ ) and myopes score was  $4.00 \pm 0.28$  ( $p=0.0001$ ). On 3<sup>rd</sup> month the score was similar  $4.68 \pm 0.44$  ( $p=0.0001$ ) in hyperopic patients and  $3.89 \pm 0.48$  ( $p=0.0009$ ) in myopes, respectively.

Finally, on the 6<sup>th</sup> month postoperatively, score was following:  $4.48 \pm 0.69$  (min 3, max 5) in hyperopes and  $3.54 \pm 0.79$  (min 2, max 4) in myopes, respectively. Beside statistical difference with preoperative values ( $p=0.0001$ ,  $p=0.0001$ ), the difference between two groups of hyperopes and myopes was also statistically significant ( $p=0.008$ ).

Table 6. Patient satisfaction score 1-5, comparison between myopes and hyperopes 6 months postoperatively.

	Patient satisfaction (1-5)
<b>Hyperopes</b>	4.48+/-0.69 (3-5)
<b>Myopes</b>	3.54+/-0.79 (2-4)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistical significant</b>	*p=0.008

Figure 12. Patient satisfaction in hyperopes and myopes 6 months postoperatively.



### 5.1.5. COMPLICATIONS MFIOL GROUP

Two patients (2%) developed cystoid macular edema (CME) observed at one month follow up and were treated with corticosteroid and/or non-steroid anti-inflammatory drops and/or corticosteroid parabolbar injections, which resolved after three months. Five patients (5%) had a mild PCO on the control exam after three months and had laser capsulotomy done.

Three patients (3%) developed high intraocular pressure (IOP) as corticosteroid responders, but were taken off corticosteroids and put on non-steroid anti-inflammatory drops along with temporary anti-glaucoma drops.

Neither complication had a permanent effect on visual acuity or patient satisfaction.

### **5.1.6. SUMMARY MFIOL GROUP**

Postoperative manifest refraction SE in both hyperopes (0.38D) and myopes (0.32D) was satisfactory and statistically significant as compared to preoperative values (1.81D, -5.14D, respectively). There was no statistical significance between two groups. Both of the groups were in slightly plus diopter which was a more natural condition for the hyperopes than myopes. Postoperative uncorrected near visual acuity at 6 months was, however, statistically better in hyperopes as compared to myopes (1.16 versus 1.43,  $p=2.88E-05$ ). There was no statistical significance between hyperopes (0.95) and myopes (0.94) at the six month point in uncorrected distance visual acuity ( $p=0.43$ ). At 6 months postoperatively, 55.84% hyperopes and 44.16% myopes were “very satisfied”, which was statistically significant difference between groups ( $p=0.008$ ).

## **5.2. LASER IN SITU KERATOMILEUSIS - LASIK GROUP**

A total of 198 eyes (99 patients) were included in the LASIK group. There were 100 eyes (50 patients) with hypermetropia and 98 eyes (49 patients) with myopia who underwent LASIK surgery. The average age of the group was  $48.8\pm 2.98$  years old, 51% female, 49% male, all Caucasian. Patients were followed up for 6 months on time points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month, 3<sup>rd</sup> month and finally 6<sup>th</sup> month when manifested refraction in spherical equivalent, uncorrected near and distant visual acuity, best corrected near and distant visual acuity, were analyzed and statistically compared. Patient satisfaction questionnaire was given preoperatively and on 1<sup>st</sup> month, 3<sup>rd</sup> month and 6<sup>th</sup> month.

### **5.2.1. MANIFESTED REFRACTION SPHERICAL EQUIVALENT**

Preoperatively, mean spherical equivalent was for hyperopes  $4.28\pm 1.03D$  (min 3, max 7.25) and for myopes  $-4.61\pm 1.14D$  (min -3.00, max -7.25), while overall spherical equivalent was  $-0.12\pm 4.59D$  (min -7.25, max 7.25). Six months postoperatively, mean spherical equivalent for hyperopes was  $0.51\pm 0.53D$  (min -0.88, max 1.75) and for

myopes  $-0.61 \pm 0.37D$  (min  $-1.75$ , max  $0$ ), which was statistically significant as compared to preoperative values in both groups ( $p < 0.05$ ).

There were also statistically significant differences between hyperopes and myopes in manifest refraction after 6 months ( $p = 9.60E-36$ ).

Mean hyperopic group spherical equivalent in other following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were  $0.50 \pm 0.70D$ ,  $0.55 \pm 0.60D$ ,  $0.49 \pm 0.78D$  and  $0.50 \pm 0.75D$ , respectively, which were all statistically significant as compared to preoperative values ( $p < 0.05$ ).

Mean myopic group spherical equivalent in all following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were  $-0.35 \pm 0.50D$ ,  $-0.45 \pm 0.54D$ ,  $-0.53 \pm 0.51D$  and  $-0.55 \pm 0.60D$ , respectively, which were all statistically significant as compared to preoperative values ( $p < 0.05$ ).

Table 7. Manifested refraction SE (diopters) comparison between hyperopes and myopes. SDEV (standard deviation).

	Manifest refraction SE (diopters/mean±SDEV(min-max))	
	Preop	6 months
<b>Hyperopes</b>	$4.28 \pm 1.03$ (3-7.25)	$0.51 \pm 0.53$ (-0.88-1.75)
<b>Myopes</b>	$-4.61 \pm 1.14$ (-3.00- -7.25)	$-0.61 \pm 0.37$ (-1.75-0)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistically significant</b>	$p = 10.63E-47$	$p = 9.60E-36$

Figure 13. Manifested refraction in hyperopes preoperatively (preop) and 6 months postoperatively (postop).

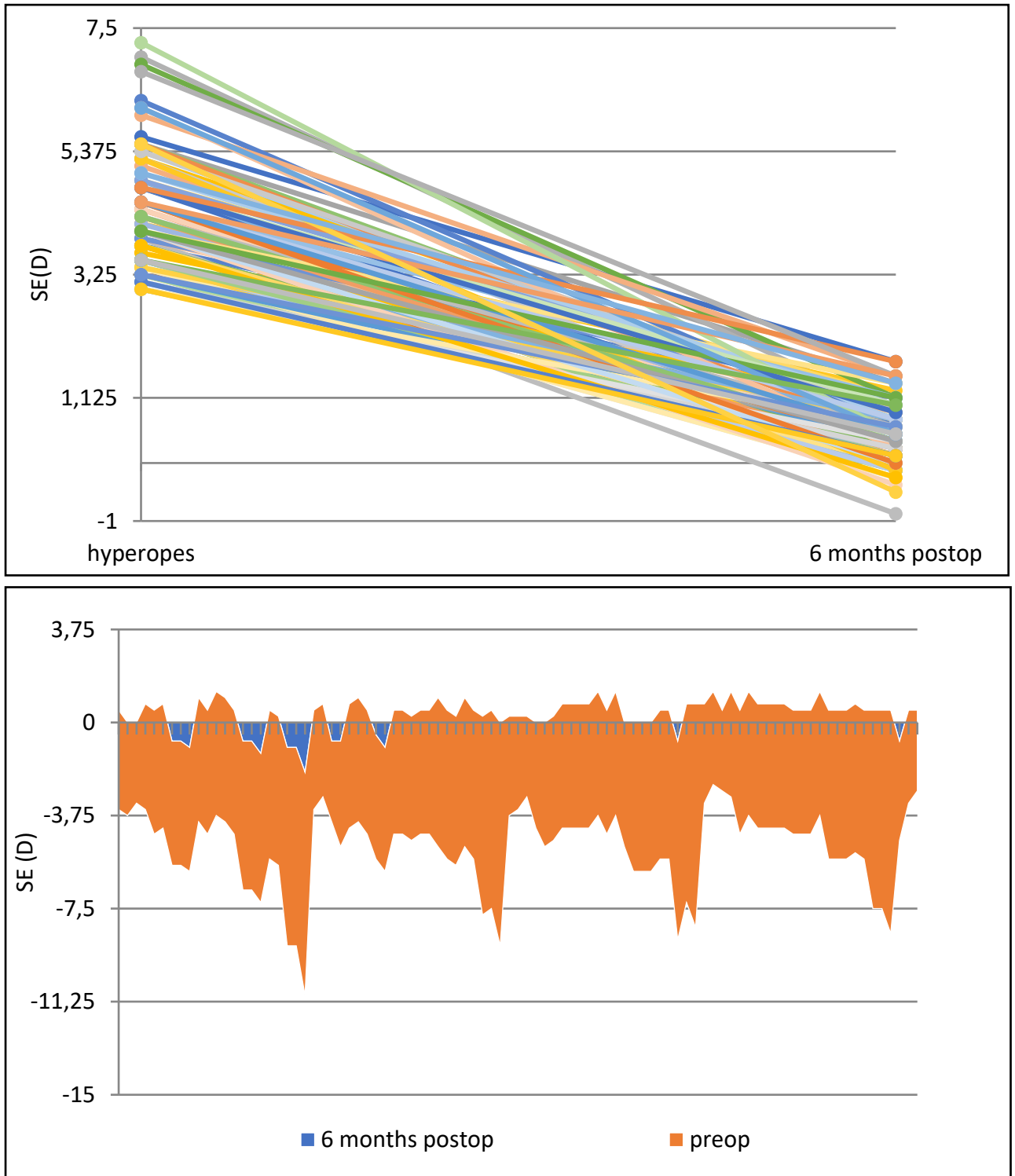
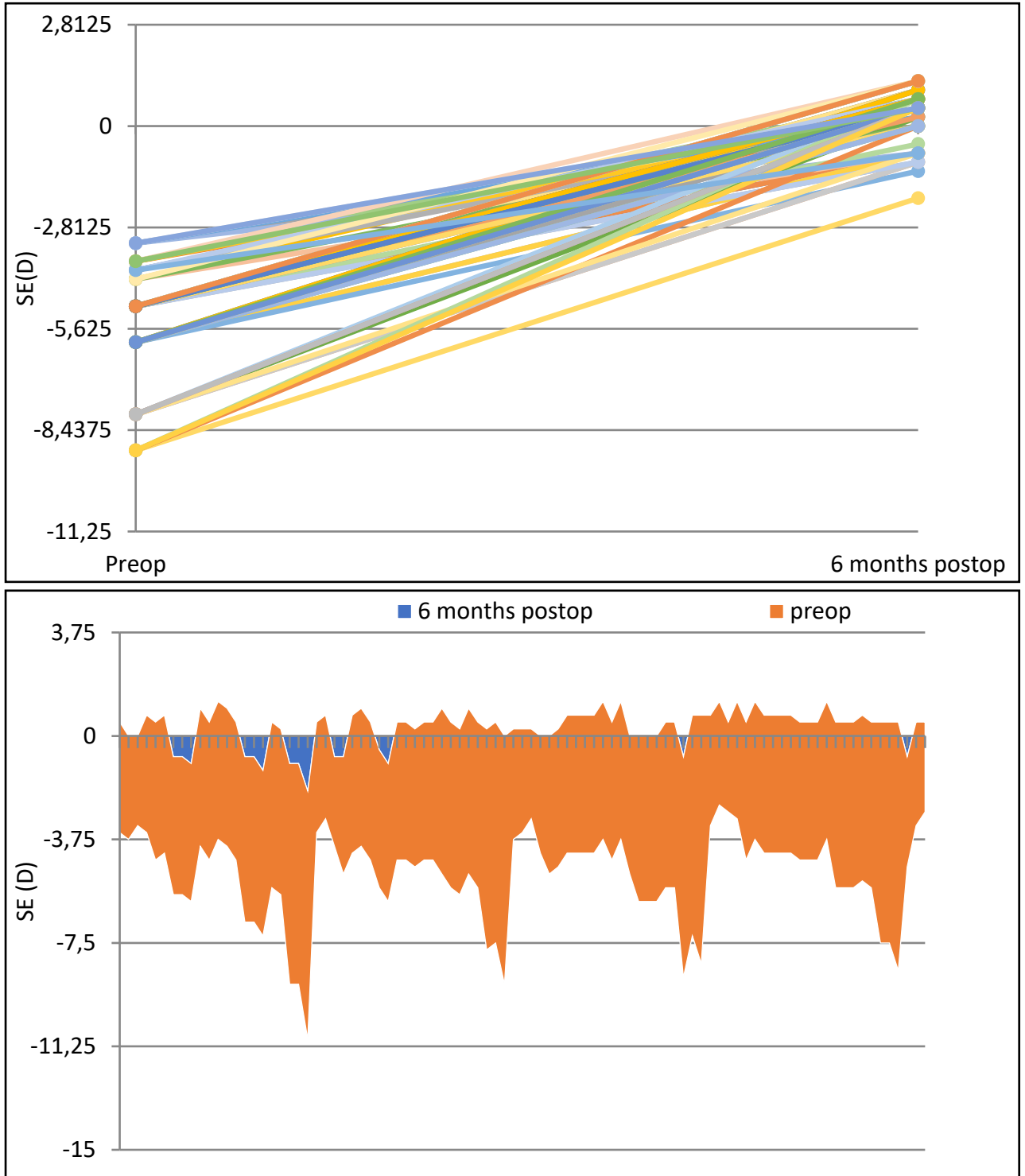


Figure 14. Manifested refraction in myopes preoperatively (preop) and 6 months postoperatively (postop).



### 5.2.2. UNCORRECTED AND BEST CORRECTED NEAR VISUAL ACUITY

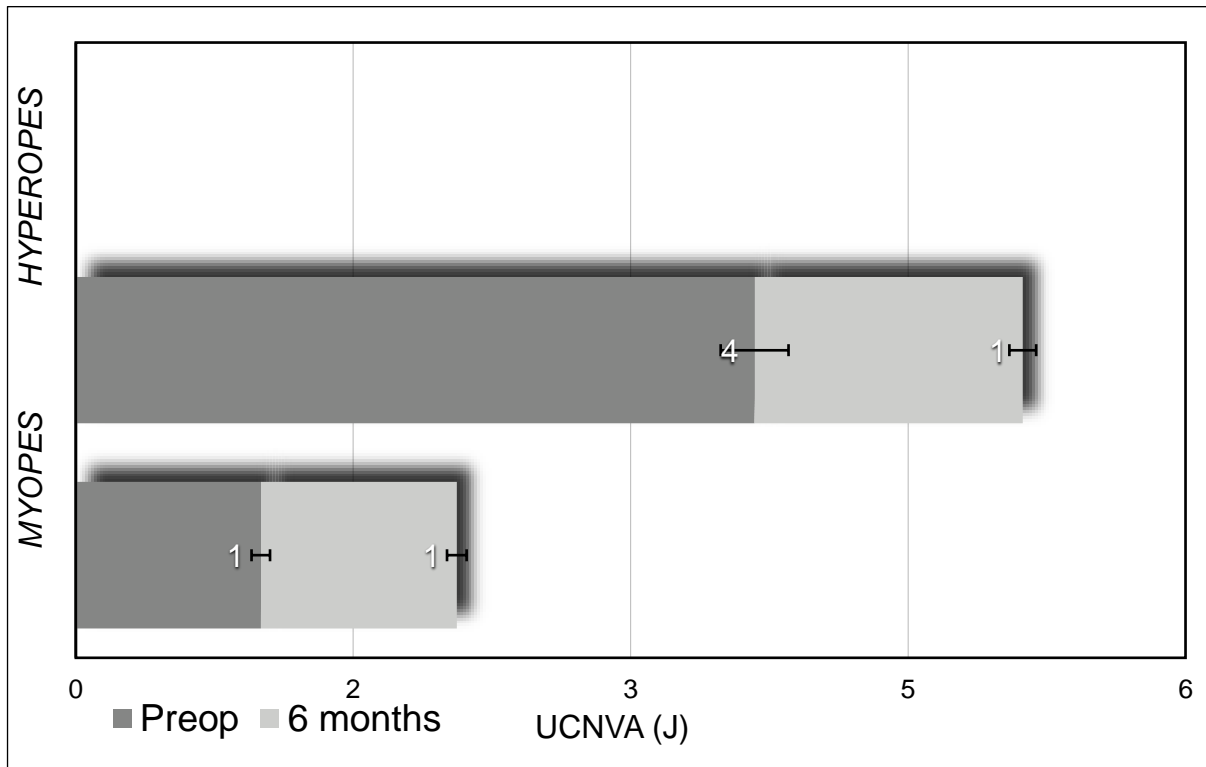
Mean preoperative uncorrected near visual acuity was in hyperopes 3.67±0.90J (min 2, max 5) while in myopes 1.00±0.00J (min 1, max 1). Overall, uncorrected near visual acuity was 2.34±1.48J (min 1, max 5). Six months postoperatively, uncorrected near visual acuity was 1.45±0.62J (min 1, max 3) in hyperopic eyes and 1.06±0.23J (min 1, max 2) in myopic eyes, respectively, which was statistically significant as compared to preoperative values in hyperopes, but not in myopes (p=1.48E-15, p=0.50). There was also statistical significance between hyperopes and myopes at the six months point (p=1.72E-07). Mean hyperopic group uncorrected near visual acuity in the other following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were 1.51±0.70J, 1.50±0.80J, 1.49±0.74J and 1.45±0.70J, respectively, which were all statistically significant as compared to preoperative values (p<0.05).

Mean myopic group SE in all following points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month and 3<sup>rd</sup> month were 1.14±0.50J, 1.11±0.50J, 1.11±0.55J, 1.14±0.20J and 1.10±0.55J, respectively, which were all statistically significant as compared to preoperative values (p<0.05).

Table 8. Uncorrected near visual acuity (Jaeger) comparison between hyperopes and myopes. SDEV (standard deviation).

	UCNVA (Jaeger/mean±SDEV(min-max))	
	Preop	6 months
<b>Hyperopes</b>	3.67±0.90 (2-5)	1.45±0.62 (1-3)
<b>Myopes</b>	1.00±0.00(1-1)	1.06±0.23 (1-2)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistical significant</b>	*p= 1.421E-45	*p=1.72E-07

Figure 15. Uncorrected near visual acuity (Jaeger) comparison between hyperopes and myopes preoperatively (preop) and 6 months postoperatively (postop).



Mean preoperative best corrected near visual acuity (BCNVA) was  $1.01 \pm 0.11J$  in hyperopes (min 1, max 2) while in myopes  $1.00 \pm 0.00J$  (min 1, max 1).

Overall, preoperative best corrected near visual acuity in LASIK group was  $1.01 \pm 0.08J$  (min 1, max 2). Six months postoperatively, best corrected near visual acuity in hyperopic eyes was  $1.01 \pm 0.05J$  (min 1, max 1.5) and in myopic eyes  $1.00 \pm 0.01J$  (min 1, max 1.5) which was not statistically different as compared to preoperative values nor in comparison of groups. The similar trend was seen in all other time points.



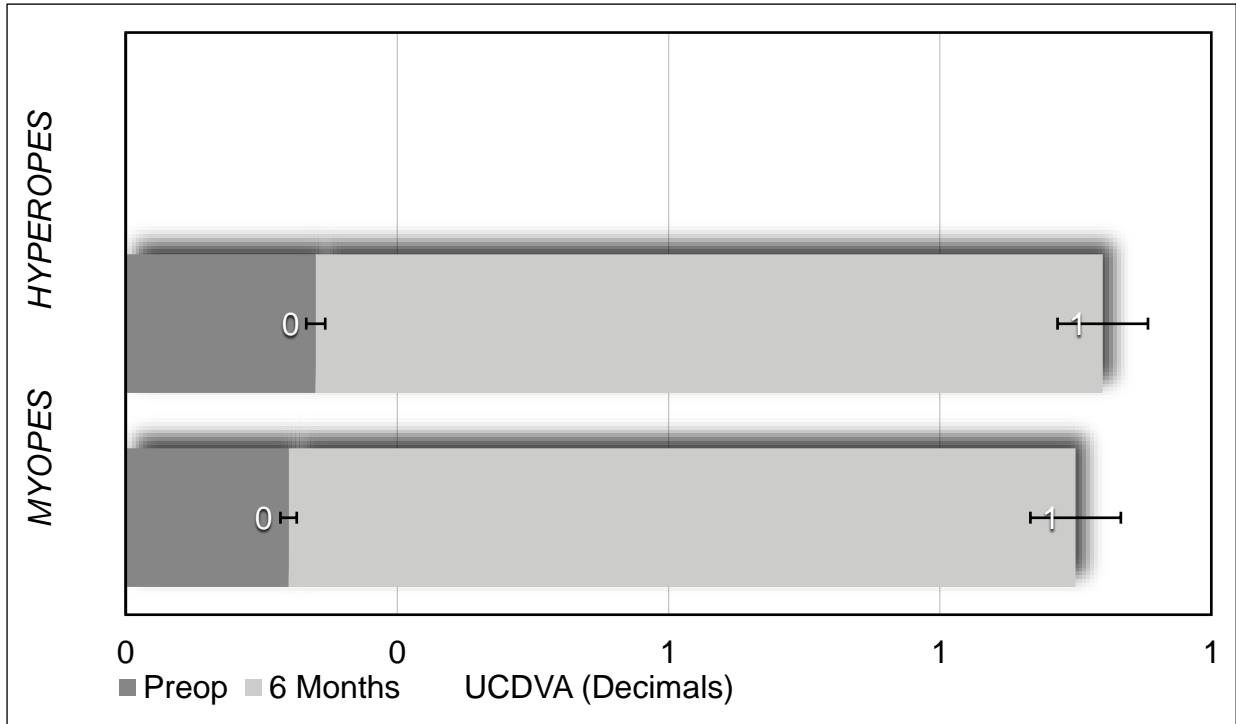
### 5.2.3. UNCORRECTED AND BEST CORRECTED DISTANT VISUAL ACUITY

Mean preoperative uncorrected distant visual acuity (UCDVA) was in hyperopes  $0.21 \pm 0.14D$  (min 0.02, max 0.80), while in myopes  $0.18 \pm 0.12D$  (min 0.03, max 0.60). Overall uncorrected distant visual acuity was  $0.19 \pm 0.13D$  (min 0.02, max 0.80). Six months postoperatively uncorrected distant visual acuity was  $0.87 \pm 0.15D$  (min 0.40, max 1) in hyperopic eyes and  $0.87 \pm 0.17D$  (min 0.30, max 1) in myopic eyes, respectively, which was statistically significant as compared to preoperative values in both groups ( $p=8.47E-32$ ,  $p=8.89E-32$ ). There was no statistical significance between hyperopes and myopes at six months point ( $p=0.88$ ).

Table 9. Uncorrected distant visual acuity (decimals) comparison between hyperopes and myopes. SDEV (standard deviation).

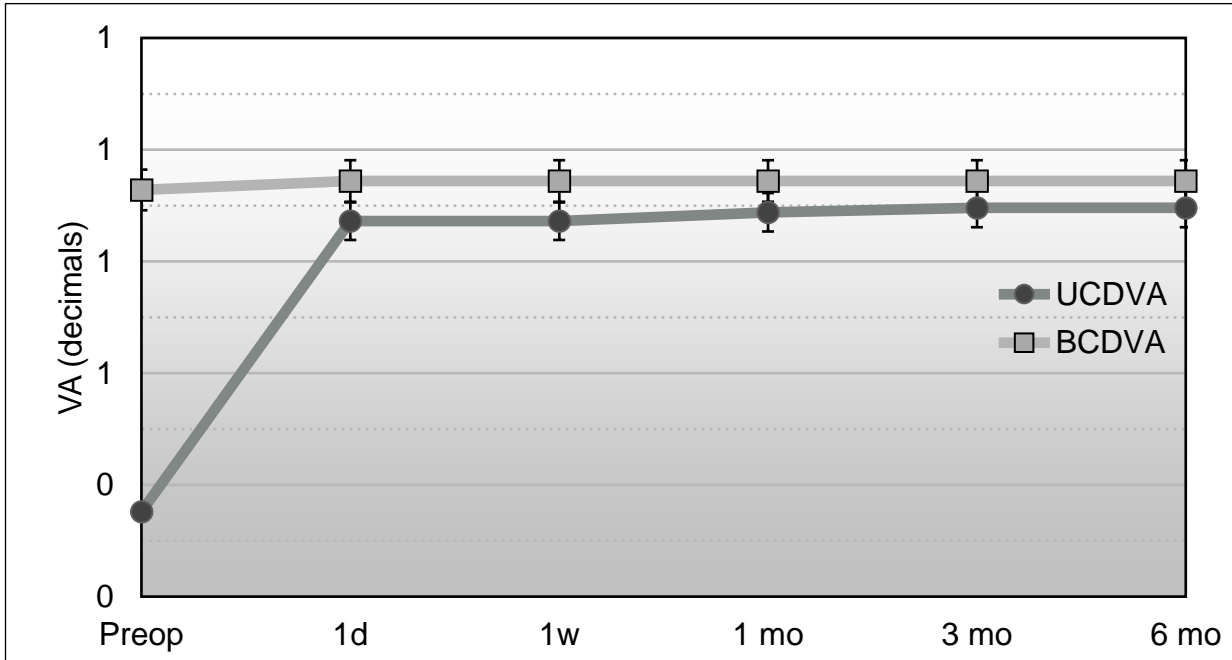
	UCDVA (decimals/mean±SDEV(min-max))	
	preop	6 months
<b>Hyperopes</b>	$0.21 \pm 0.14$ (0.02-0.80)	$0.87 \pm 0.15$ (0.40-1)
<b>Myopes</b>	$0.18 \pm 0.12$ (0.03-0.60)	$0.87 \pm 0.17$ (0.30-1)
<b>Student t test (2 sample unequal) *<math>p &lt; 0.05</math> statistical significant</b>	$p = 0.06$	$p = 0.88$

Figure 16. UCDVA (decimals) comparison between hyperopes and myopes preoperatively (preop) and 6 months postoperatively (postop).



Mean preoperative best corrected distant visual acuity (BCDVA) was  $0.87 \pm 0.13D$  in hyperopes (min 0.40, max 1.0) while in myopes was  $0.95 \pm 0.11D$  (min 0.40, max 1). Overall preoperative best corrected distant visual acuity in LASIK group was  $0.91 \pm 0.11D$  (min 0.40, max 1). Six months postoperatively best corrected distant visual acuity in hyperopic eyes was  $0.91 \pm 0.01D$  (min 0.65, max 1) and in myopic eyes was  $0.93 \pm 0.03D$  (min 0.85, max 1) which was not statistically different as compared to preoperative values nor in comparison of groups. The similar trend was in all other time points. Overall uncorrected distant visual acuity and best corrected distant visual acuity change over time in LASIK group.

Figure 17. UCDVA and BCDVA (decimals) throughout time (follow up 6 months). UCDVA (uncorrected distant visual acuity), BCDVA (best corrected distant visual acuity), VA (visual acuity), d (day), w (week), mo (month).



### 5.2.4. PATIENTS SATISFACTION

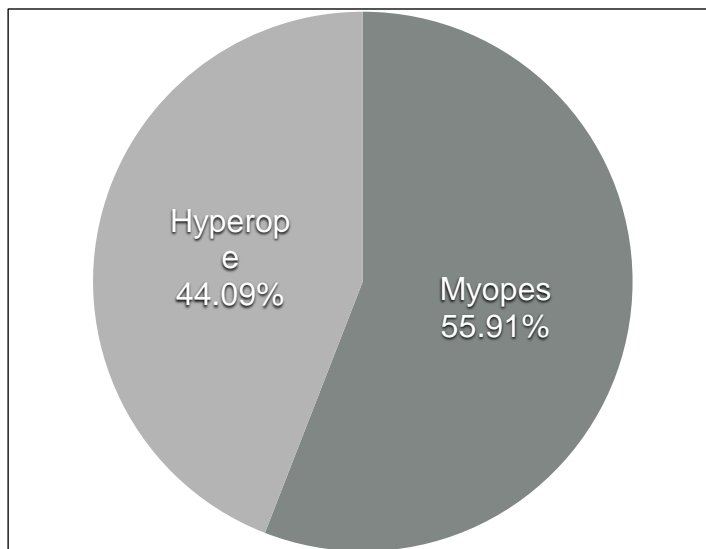
Patient satisfaction questionnaire was given preoperatively and on 1<sup>st</sup> month, 3<sup>rd</sup> month and 6<sup>th</sup> month. The score was from 1-5, 1 meaning “not satisfied”, 5 meaning “very satisfied”. Preoperatively, mean results in hyperopic eyes were  $2.00 \pm 0.71$ , while in myopic eyes were  $2.00 \pm 0.45$ . On 1<sup>st</sup> month, hyperopes were significantly satisfied, as the score was  $3.69 \pm 0.32$  ( $p=0.0001$ ) and score for myopes was  $4.01 \pm 0.24$  ( $p=0.00009$ ). On 3<sup>rd</sup> month results were similar, with  $3.68 \pm 0.35$  ( $p=0.0001$ ) in hyperopic patients and  $4.49 \pm 0.48$  ( $p=0.00009$ ) in myopes, respectively.

Finally, six months postoperatively, results were following:  $3.58 \pm 0.59$  (min 2, max 4) in hyperopes and  $4.54 \pm 0.79$  (min 3, max 4) in myopes, respectively. Beside statistical difference with preoperative values ( $p=0.0001$ ,  $p=0.00009$ ), the difference between two groups of hyperopes and myopes was also statistically significant ( $p=0.01$ ).

Table 10. Patient satisfaction 1-5 (1-not satisfied, 5-very satisfied), comparison between hyperopes and myopes 6 months postoperatively.

	Patient satisfaction (1-5)
<b>Hyperopes</b>	3.58±0.59 (2-4)
<b>Myopes</b>	4.54±0.89 (3-5)
<b>Student t test (2 sample unequal) *p&lt;0.05 statistical significant</b>	*p=0.01

Figure 18. Patient satisfaction in hyperopes and myopes 6 months postoperatively.



### **5.2.5. COMPLICATIONS LASIK GROUP**

Two patients (4%) in hyperopic group of 50 patients had a return of hypermetropia of 2D and 1.5D SE, respectively, at the 3<sup>rd</sup> month follow up and were re-operated after 6 months postoperatively. One patient (1.01%) in overall LASIK group of 99 patients developed diffuse lamellar keratitis (DLK) and was treated with corticosteroid drops, with resolution by 3<sup>rd</sup> month of follow up. Five patients (5.05%) had dry eye syndrome and were treated accordingly. Two patients (2.02%) developed high intraocular pressure as corticosteroid responders, but were taken off corticosteroids and put on non-steroid anti-inflammatory drops along with temporary anti-glaucoma drops. Neither complications had a permanent effect on visual acuity.

### **5.2.6. SUMMARY LASIK GROUP**

Postoperative manifest refraction SE in both hyperopes (0.51D) and myopes (-0.61D) was satisfactory and statistically significant as compared to preoperative values (4.28D, -4.61D), respectively. There was statistical difference between the two groups ( $p=9.60E-36$ ). Hyperopes group was in slightly plus diopter because they often have cycloplegia refraction in much bigger plus, which we try to compensate maximally by putting the maximal plus diopter in the laser which they can tolerate.

Myopes were in slightly minus because we usually put the minimal minus diopter value for laser ablation, as they cannot be hypercorrected and we always fear of reversion in plus diopter, which myopes have no tolerance, as they can hardly compensate for near visual acuity.

Surprisingly, postoperative uncorrected near visual acuity at 6 months was statistically better in myopes as compared to hyperopes (1.06 versus 1.45,  $p=1.72E-07$ ). There was no statistical significance between hyperopes (0.87) and myopes (0.87) at the six month point in uncorrected distant visual acuity ( $p=0.88$ ). At 6 months postoperatively, 44.09% hyperopes and 55.91% myopes were “very satisfied”, which was statistically significant difference between groups ( $p=0.01$ ).

### 5.3. COMPARISON OF MFIOL AND LASIK GROUP

Both groups of patients with presbyopia, with average age in MFIOL group of 52 years old, and in LASIK 48.8 years old. They were divided into subgroups of hyperopes and myopes because of easier comparison, in order to determine and upgrade the current protocol in the choice of refractive surgery. Our patients were not randomized in either group (MFIOL or LASIK), they were predetermined based on our current protocols, patient's life style and wishes in either of the group. We wanted to investigate whether there is any difference in the visual performance and their satisfaction, so we can upgrade our recommendations in preoperative evaluation of MFIOL versus LASIK.

Thus, when comparing hyperopes in MFIOL group versus LASIK group, we observed:

1. Manifest refraction in MFIOL group was  $0.38 \pm 0.79D$  (0.75-1.25) as compared to  $0.51 \pm 0.53D$  (-0.88-1.75) in LASIK group 6 months postoperatively, which was not statistically significant ( $p=0.08$ ).
2. Six months postoperatively uncorrected near visual acuity in MFIOL was  $1.16 \pm 0.37J$  (1-2) as compared to  $1.45 \pm 0.62J$  (1-3) in LASIK group, which was statistically significant ( $p=0.0002$ ). MFIOL group had statistically better uncorrected near visual acuity than LASIK group.
3. Six months postoperatively uncorrected distant visual acuity was greater in MFIOL group with  $0.95 \pm 0.07D$  (0.65-1) as compared to  $0.87 \pm 0.15D$  (0.40-1) in LASIK group, which was statistically significant ( $p=0.000004$ ).
4. Patient satisfaction score in MFIOL group was  $4.48 \pm 0.69$  (3-5) as compared to  $3.58 \pm 0.59$  (2-4) in LASIK group, which was statistically significant ( $p=0.01$ ).

When comparing myopes in MFIOL group versus LASIK group, we observed:

1. Manifest refraction in MFIOL group was  $0.32 \pm 0.65D$  (1.25-2.00) as compared to  $-0.61 \pm 0.37D$  (-1.75-0) in LASIK group 6 months postoperatively, which was statistically significant ( $p=3.72E-23$ ). Myopes in LASIK group were in slightly more minus than in MFIOL group.
2. Six months postoperatively uncorrected near visual acuity in MFIOL was  $1.43 \pm 0.47$  (1-3) as compared to  $1.06 \pm 0.23$  (1-2) in LASIK group, which was statistically significant ( $p=5.59E-10$ ). LASIK group had statistically better uncorrected near visual acuity than MFIOL group.
3. Six months postoperatively uncorrected distant visual acuity was greater in MFIOL group with  $0.94 \pm 0.08$  (0.65-1) as compared to  $0.87 \pm 0.17$  (0.30-1) in LASIK group, which was statistically significant ( $p=0.000003$ ).
4. Patient satisfaction score in MFIOL group was  $3.54 \pm 0.79$  (2-4) as compared to  $4.54 \pm 0.89$  (3-5) in LASIK group, which was statistically significant ( $p=0.009$ ). Myopes in LASIK group were more satisfied than myopes in MFIOL group.

## 6. DISCUSSION

Presbyopia is an age-related eye condition where one of the signs is the reduction in the amplitude of accommodation, resulting in loss of the ability to change the eye's focus from far to near. Loss of near focusing ability that occurs with age, most people begin to notice after 40 years of age, when they start having trouble seeing small print clearly. Presbyopia occurs when the lens loses its normal accommodating power and can no longer focus on objects viewed at arm's length or closer. Symptoms of presbyopia is holding reading material farther from your eyes to see them more clearly, eye strain, headaches or visual fatigue from doing close work.

Methods for presbyopia correction include contact lens and spectacles as treatment options, however, the surgical correction of presbyopia still remains a significant challenge for refractive surgeons. Surgical strategies for dealing with presbyopia may be extraocular (corneal or scleral) or intraocular (removal and replacement of the crystalline lens or some type of treatment on the crystalline lens itself).<sup>89</sup> There are, however, a number of limitations and considerations that have limited widespread acceptance of surgical correction of presbyopia. The preoperative manifest refraction is, for one, very important factor in deciding which surgery can be performed, as well as the lifestyle of the patients and their expectations of postoperative vision results. Therefore, each surgical strategy presents its own unique set of advantages and disadvantages. In our clinical practice, we have acquired certain experienced knowledge along with appropriate surgical recommendations for different approaches and technology used for our patients.

In this study, we followed, for six months, two groups of patients, the age of 45-55 years old who underwent either refractive lens exchange treatment on lens with multifocal intraocular lens implantation or Laser in Situ Keratomileusis procedure on cornea. Our patients were not plano presbyopia patients, as they had a refractive error as inclusion criteria for myopic patients with  $\geq -3.0D$  and for hyperopic patients with  $\geq +1.00D$  of spherical equivalent with astigmatism less than 1D. They could not have had a cataract or any other ocular disease on the cornea or retina or systemic disease. As well as unremarkable corneal topography. Plano presbyopia patients were not included in the study because our primary focus was on a specific subgroup of the population, hyperopes or myopes in their forties, that are not comfortable with using



multiple pairs of glasses for distant, intermediate and near vision, but also still don't have a cataract which would otherwise put them straight into the MFIOL group.

The MFIOL we chose were diffractive Acryva Reviol lenses (VSY Biotechnology, Amsterdam, Netherlands), where performance is based on their establishment of diffractive zones. The different number, height, interval and width of the rings affect patient total visual outcomes under lower light conditions.

Diffractive multifocal IOL engineering is based on balanced light energy between foci. Narrow rings increase the near addition. Conversely, higher steps enable the transfer of more energy to near focus.<sup>90</sup> Most studies report good and stable distance vision and near vision, leading to low spectacle dependence and high patient satisfaction.<sup>91,92</sup> Although these designs have good visual outcomes, their weakest points can be their inability to provide good levels of vision at an intermediate distance and loss of contrast sensitivity (CS). However, Acryva Reviol lens has been reported with increased CS, as it's diffractive optic preserves a better balance of 60% far and 40% near focus at 6 mm pupil aperture. Balanced light distribution under any light condition increases contrast sensitivity.<sup>93-95</sup>

LASIK was performed by standardized procedure of excimer laser (Schwind, Amaris).

Each patient underwent thorough preoperative examination along with the lifestyles type of questioning and their expectations. They have also completed patient's satisfaction questionnaire regarding their visual activities and satisfaction after procedures.

The two main groups: MFIOL group and LASIK group, were additionally subdivided into hyperopes and myopes because of their different characteristics and easier follow up. In our results, we found that hyperopes had statistically better uncorrected near visual acuity and uncorrected distance visual acuity in MFIOL group, and myopes had better uncorrected near visual acuity in LASIK groups. Uncorrected distance visual acuity in myopes was statistically lower in LASIK group which can be explained by slight myopization in uncorrected distance visual acuity, where we put minimal minus for laser ablation in order not to get plus in myopes, which they poorly tolerate. On the other hand, in the MFIOL group, myopes had slight plus (0.32D) of manifest refraction where we attempted to put them close to zero diopter in calculations of dominant eye for distance.

It is important to emphasize that in MFIOL group we did not do monovision surgery and deliberately put one non-dominant eye in slight minus.

According to our clinical experience and with the scientific references in calculating the lens, we targeted to obtain emmetropia in both myopes and hyperopes, while having in mind which eye is dominant. On the contrary, hyperopes LASIK group was in slightly plus diopter because they often have much greater cycloplegia refraction, even though we try to compensate it by performing the laser ablation of the maximal plus diopter, which they can tolerate. In fact, two patients (4%) in hyperopic LASIK group therefore had the regression of hypermetropia of 2D and 1.5D SE, respectively, at 3<sup>rd</sup> month follow up and were re-operated after 6 months of follow up.

On the other hand, hyperopes tolerated slight plus very well in MFIOL group for uncorrected distance visual acuity and their uncorrected near visual acuity was statistically significantly better than in myopes MFIOL group. However, uncorrected near visual acuity in hyperopes MFIOL was also better than in LASIK group hyperopes. This could be explained by the fact of weaker hyperopic accommodation properties generally and especially in their forties as compared to myopes.

Hyperopes have to exercise the level of their accommodation for distant vision as well as for near, so their tolerance, even after hypermetropic ablation, is more debilitated in LASIK group as compared to MFIOL group, where a diffractive lens replaces the accommodative apparatus.<sup>96</sup>

Thus, accordingly to results, patient satisfaction questionnaire followed. The hyperopes were more satisfied in MFIOL group and myopes in LASIK group, and the satisfaction score was statistically different ( $p=0.01$ ,  $p=0.009$ ), respectively between groups. When comparing scores throughout time points, both MFIOL and LASIK groups of hyperopes and myopes had the highest scores on 1<sup>st</sup> and 3<sup>th</sup> month because of so-called “wow” effect of refractive surgery as well as refractive error resolution. Later, the score was smaller but still in consistence with the overall result. That could be explained by developing a habit of new vision, dry eye in LASIK group, and in 5 patients in MFIOL group by developing a very mild posterior capsular opacification, which nevertheless was treated with laser capsulotomy.

Recent studies concluded that the most important intraocular lens related factor in preventing posterior capsular opacification formation is a square edge on the posterior optic surface of the intraocular lens, exerting a mechanical barrier effect which is the

exact property of Acriva lens. This could explain such a low rate of posterior capsular opacification even though the patient were relatively young and therefore more prone to that formation.<sup>97,98</sup>

Other visual disturbances as halos and glares were not reported and were very well tolerated, as sharper transition zones interact with photic phenomena in these lenses.

## 7. CONCLUSION

This research had fulfilled the pre-proposed aims and purposes.

1. Both MFIOL implantation and LASIK surgical procedures had proven to be effective and safe with a low rate of complications. Overall manifest refraction as well as manifest refraction in subgroups of hyperopes and myopes in both procedures were significantly decreased 6 months postoperatively.
2. Uncorrected near visual acuity was statistically different between subgroups of hyperopes and myopes in MFIOL group and in LASIK group. Uncorrected near visual acuity in hyperopes group was statistically better than uncorrected near visual acuity in myopic group in the MFIOL procedure. However, in LASIK group it was vice versa in favor of myopes. Additionally, there was statistical difference between uncorrected near visual acuity of hyperopes in MFIOL versus hyperopes in LASIK group, and myopes in MFIOL versus myopes in LASIK group. The hyperopes in MFIOL group had better uncorrected near visual acuity than in LASIK group. Similarly, myopes in LASIK group had better uncorrected near visual acuity than myopes in MFIOL group.
3. There was no statistical significance between subgroups of hyperopes and myopes at the six month point in uncorrected distant visual acuity in either MFIOL or LASIK group. However, uncorrected distant visual acuity was statistically better in both hyperopes and myopes in MFIOL group than hyperopes and myopes in LASIK group.
4. Postoperative mean residual manifest refraction in both hyperopes and myopes in MFIOL group was in slightly plus diopter, which was more natural condition for the hyperopes than myopes and could have influenced hyperopes positive satisfaction rate in MFIOL group. On the contrary, in LASIK group myopes were in mean minus diopter of SE postoperatively that enabled them to get better uncorrected near visual acuity than myopes in MFIOL group, thus getting a better satisfactory rate after LASIK procedure. Hyperopes in LASIK group were in slight plus residual refraction and were not satisfied with uncorrected near visual acuity as compared to MFIOL group due to accommodation problems.

5. Hyperopes were more satisfied than myopes in MFIOL group and hyperopes in LASIK group. Myopes were more satisfied than hyperopes in LASIK group and myopes in MFIOL group. This was affirmed also by the patient satisfaction questionnaire.
6. This research would be of great help in future screening of patients for the different surgical procedures of MFIOL versus LASIK. Hyperopic patients (who meet the criteria in the presbyopia age from 45-55 years old) would rather be suggested for MFIOL implantation than LASIK, and myopic patients are more suitable for LASIK.

## 8. SUMMARY

Title: Presbyopia treatment lens surgery versus Laser in situ keratomileusis

Author: Adis Pašalić

Zagreb, 2020.

**PURPOSE:** To evaluate the effectiveness in presbyopia treatment of two surgical methods: lens surgery versus Laser in situ keratomileusis

**METHODS:** Patients were separated into two groups according to the surgical procedure which they were treated — lens surgery with multifocal intraocular lens implantation (MFIOL group) and Lasik in situ keratomileusis procedure on the cornea (LASIK group). Within each group, the treated eyes were further subdivided according to the type of diopter: myopic or hypermetropic patients. A total of 200 eyes (100 patients) were included in the MFIOL group. There were 110 eyes (54 patients) with hypermetropia and 90 eyes (45 patients) with myopia who underwent lens surgery. A total of 198 eyes (99 patients) were included in the Lasik in situ keratomileusis group. There were 98 eyes (49 patients) with hypermetropia and 100 eyes (50 patients) with myopia. Patients were followed up for 6 months on time points 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month, 3<sup>rd</sup> month and finally 6<sup>th</sup> month, when manifested refraction in spherical equivalent (SE), uncorrected near visual acuity and uncorrected distant visual acuity (UCNVA, UCDVA), best corrected near visual acuity and best corrected distant visual acuity (BCNVA, BCDVA), were analyzed and statistically compared. Satisfaction questionnaire was given preoperatively and on 1<sup>st</sup> month, 3<sup>rd</sup> month and 6<sup>th</sup> month postoperatively.

**RESULTS:** Both groups of patients were presbyopes with average age in MFIOL group of 52 years, and in LASIK 48,8 years old, respectively. Thus, when comparing hyperopes in MFIOL group versus LASIK group we observed:

1. Manifest refraction in MFIOL was  $0.38 \pm 0.79D$  (0.75-1.25) as compared to  $0.51 \pm 0.53D$  (-0.88-1.75) in LASIK 6 months postoperatively, which was not statistically significant ( $p=0.08$ ). 2. Six months postoperative UCNVA in MFIOL was

1.16±0.37J (1-2) versus 1.45±0.62J (1-3) in LASIK group, which was statistically significant (p=0.0002). MFIOL group had statistically better UCNVA than LASIK group. 3. Six months postoperative UCDVA was greater in MFIOL with 0.95±0.07 (0.65-1) versus 0.87±0.15 (0.40-1) in LASIK group, which was statistically significant (p=0.000004). 4. Patients satisfaction score in MFIOL group was 4.48±0.69 (3-5) versus 3.58±0.59 (2-4) in LASIK group, which was statistically significant (p=0.01).

When comparing myopes in MFIOL group versus LASIK group we observed:

1. Manifest refraction in MFIOL was 0.32±0.65D (1.25-2.00) as compared to -0.61±0.37D (-1.75-0) in LASIK 6 months postoperatively, which was statistically significant (p=3.72E-23). LASIK myopes were in slightly more minus diopter than MFIOL group. 2. Six months postoperative UCNVA in MFIOL was 1.43±0.47 (1-3) versus 1.06±0.23 (1-2) in LASIK group, which was statistically significant (p=5.59E-10). LASIK group had statistically better UCNVA than MFIOL group. 3. Six months postoperative UCDVA was greater in MFIOL with 0.94±0.08 (0.65-1) versus 0.87±0.17 (0.30-1) in LASIK group, which was statistically significant (p=0.000003). 4. Patient satisfaction score in MFIOL group was 3.54±0.79 (2-4) versus 4.54±0.89 (3-5) in LASIK group, which was statistically significant (p=0.009). Myopes in LASIK group were more satisfied than myopes in MFIOL group.

**CONCLUSION:** Both surgical procedures: MFIOL implantation and LASIK surgical procedures had proven to be effective and safe with a low rate of complications. Overall manifest refraction as well as manifest refraction in subgroups of hyperopes and myopes in both procedures were significantly decreased 6 months postoperatively. Uncorrected near visual acuity was statistically different between subgroups of hyperopes and myopes in MFIOL group and in LASIK group. uncorrected near visual acuity in hyperopic group was statistically better than uncorrected near visual acuity in myopic group in the MFIOL procedure. However, in LASIK group it was vice versa in favor of myopes.

Additionally, there was statistical difference between uncorrected near visual acuity of hyperopes in MFIOL versus hyperopes in LASIK group, and myopes in MFIOL versus myopes in LASIK group. The hyperopes in MFIOL group had better uncorrected near visual acuity than in LASIK group. Similarly, myopes in LASIK group had better uncorrected near visual acuity than myopes in MFIOL group.

## 9. SAŽETAK

Naslov: Tretman prezbiopije: kirurgija leće u odnosu na Laser in situ keratomileuza

Autor: Adis Pašalić

Zagreb, 2020.

CILJ: Evaluirati učinkovitost dviju kirurških metoda u tretmanu prezbiopije: kirurgija leće u odnosu na Laser in situ keratomileuzu.

METODE: Pacijenti su podijeljeni u dvije grupe prema kirurškoj metodi kojoj su podvrgnuti - kirurgija leće s ugradnjom multifokalnih intraokularnih leća (MFIOL grupa) i kirurška procedura na rožnici Laser in situ keratomileuza (LASIK grupa). U svakoj grupi tretirane oči su dalje podijeljene prema vrsti dioptrije na kratkovidne i dalekovidne pacijente. Ukupno 200 očiju (100 pacijenata) je uključeno u MFIOL grupu. Od toga je bilo 110 očiju (55 pacijenta) sa dalekovidnošću i 90 očiju (45 pacijenata) sa kratkovidnošću koji su podvrgnuti kirurgiji leće. Ukupno 198 očiju (99 pacijenata) je uključeno u LASIK grupu. Od toga je bilo 98 očiju (49 pacijenata) sa dalekovidnošću i 100 očiju (50 pacijenata) sa kratkovidnošću. Pacijenti su praćeni 6 mjeseci; prvi dan, prvi tjedan, zatim 1, 3 i 6 mjesec poslijeoperacijski, pri čemu je analizirana i statistički uspoređena manifestna refrakcija u sfernom ekvivalentu, nekorigirana vidna oštrina na blizinu i na daljinu (UCNVA, UNDVA), najbolja korigirana vidna oštrina na blizinu i daljinu (BCNVA, BCDVA). Upitnik o zadovoljstvu pacijenta popunjen je prijeoperacijski te 1, 3 i 6 mjesec poslijeoperacijski.

REZULTATI: Obje grupe pacijenata dalekovidne su na blizinu s prosječnom dobi u MFIOL grupi od 52 godine, a u LASIK grupi od 48,8 godina. Pri usporedbi dalekovidnih pacijenata u MFIOL grupi u odnosu na LASIK grupu analizirali smo i pronašli:

1). Manifestna refrakcija u MFIOL grupi je bila  $0.38 \pm 0.79D$  (0.75-1.25) u odnosu na  $0.51 \pm 0.53D$  (-0.88-1.75) u LASIK grupi 6 mjeseci poslijeoperacijski, što nema statističkog značaja, ( $p=0.08$ ). 2). Šest mjeseci poslijeoperacijski UCNVA u MFIOL grupi je bila  $1.16 \pm 0.37J$  (1-2) u usporedbi sa  $1.45 \pm 0.62J$  (1-3) u LASIK grupi, što je



statistički značajno ( $p=0.0002$ ). MFIOL grupa je imala statistički bolju UCNVA nego LASIK grupa. 3). Šest mjeseci poslijeoperacijski UCDVA je bila bolja u MFIOL grupi sa  $0.95\pm 0.07$  (0.65-1) u usporedbi sa  $0.87\pm 0.15$  (0.40-1) u LASIK grupi, što je statistički značajno ( $p=0.000004$ ). 4). Rezultat zadovoljstva pacijenta u MFIOL grupi je bio  $4.48\pm 0.69$  (3-5) u usporedbi sa  $3.58\pm 0.59$  (2-4) u LASIK grupi, što je statistički značajno ( $p=0.01$ ). Pri usporedbi kratkovidnih pacijenata u MFIOL grupi u usporedbi sa LASIK grupom analizirali smo i pronašli:

1). Manifestna refrakcija u MFIOL grupi je bila  $0.32\pm 0.65D$  (1.25-2.00) u odnosu na  $-0.61\pm 0.37D$  (-1.75-0) u LASIK grupi 6 mjeseci poslijeoperacijski, što je statistički značajno ( $p=3.72E-23$ ). 2). Šest mjeseci poslijeoperacijski UCNVA u MFIOL grupi je bila  $1.43\pm 0.47$  (1-3) u usporedbi sa  $1.06\pm 0.23$  (1-2) u LASIK grupi, što je statistički značajno ( $p=5.59E-10$ ). LASIK grupa je imala bolju statističku UCNVA u odnosu na MFIOL grupu. 3). Šest mjeseci poslijeoperacijski UCDVA je bila veća u MFIOL grupi sa  $0.94\pm 0.08$  (0.65-1) u usporedbi sa  $0.87\pm 0.17$  (0,30-1) u LASIK grupi, što je statistički značajna razlika ( $p=0.000003$ ). 4) Rezultat zadovoljstva pacijenta u MFIOL grupi je bio  $3.54\pm 0.79$  (2-4) u usporedbi sa  $4.54\pm 0.89$  (3-5) u LASIK grupi, što je bilo statistički značajno ( $p=0.009$ ). Kratkovidni pacijenti u LASIK grupi su bili više zadovoljni nego kratkovidni pacijenti u MFIOL grupi.

**ZAKLJUČAK:** Obje kirurške procedure: kirurgija leće s ugradnjom MFIOL i LASIK su pokazale učinkovitost i sigurnost s niskom učestalošću komplikacija. Sveukupna manifestna refrakcija u podgrupama dalekovidnih i kratkovidnih pacijenata u obje procedure se značajno smanjila 6 mjeseci poslijeoperacijski. Nekorigirana vidna oštrina na blizinu je statistički značajna između podgrupa dalekovidnih i kratkovidnih pacijenata u MFIOL grupi i u LASIK grupi. Nekorigirana vidna oštrina na blizinu u grupi dalekovidnih pacijenata je statistički bolja nego nekorigirana vidna oštrina na blizinu u grupi kratkovidnih pacijenata kod MFIOL-a. Međutim, u LASIK grupi bilo je obrnuto u korist kratkovidnih pacijenata. Dodatno, postoji statistički značajna razlika između nekorigirana vidna oštrina na blizinu dalekovidnih pacijenata u MFIOL grupi u odnosu na LASIK grupu i kratkovidnih pacijenata u MFIOL grupi u odnosu na LASIK grupu. Dalekovidni pacijenti u MFIOL grupi su imali bolju nekorigirana vidna oštrina na blizinu nego u LASIK grupi. Slično, kratkovidni pacijenti u LASIK grupi su imali bolju nekorigiranu vidnu oštrinu na blizinu nego kratkovidni pacijenti u MFIOL grupi.

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## 11. CURRICULUM VITAE

### Adis Pašalić, MD, ophthalmology specialist

I was born on March 25<sup>th</sup> 1981 in Zenica, Bosnia and Herzegovina. I graduated from the School of Medicine, University of Sarajevo in 2008. In 2009, I started a PhD program in Biomedicine and Health sciences at the School of Medicine, University of Zagreb, and in 2014, defended the thesis proposal with title "Presbyopia treatment lens surgery versus Laser in situ keratomileusis" under the mentorship of Prof. Iva Dekaris, MD, PhD.

I finished Specialist postgraduate study of Ophthalmology and Optometry at the School of Medicine, University of Zagreb in 2014. Since 2010, I have been working at the 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 anterior eye segment, refractive surgery, corneal transplantation and regularly participate in domestic and international ophthalmology meetings as a speaker. So far, I have published 5 scientific papers in journals indexed in Current Contents, and more than 30 congress abstracts. I am a member of the European Society for Cataract and Refractive Surgery (ESCRS), South East European Ophthalmological Society (SEEOS), European Eye Bank Association (EEBA) and Croatian Society for cataract and refractive surgery (CSCRS).