“LUCIAN BLAGA” UNIVERSITY OF SIBIU

FACULTY OF MEDICINE

PhD THESIS

SUMMARY

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“LUCIAN BLAGA” UNIVERSITY OF SIBIU

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Appearance of corneal endothelial cells after crystalline lens extraction by phacoemulsification

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1.Introduction

Ophthalmology is a fascinating surgical specialty due to the spectacular immediate postoperative outcomes. In cataract surgery, this is very obvious. The patient comes to the surgeon with a very low vision and the nest day, he goes with a very good vision, even driving the car. This is the case of cataract surgeries nowadays. But, complications can also occur, leading to patient's and surgeon's dissatisfaction. One of the most unpleasant complications includes corneal decompensation due to endothelial cell loss during surgery with repercussions on sight. This made me study the appearance of endothelial cells after crystalline lens extraction by phacoemulsification, and investigate the factors that are involved in endothelial decompensation with a view to eliminate them for better postoperative outcomes.

Cataract is one of the most common surgical eye disorders.

Clinically, cataract is the clouding of the lens leading to progressive slow decline in patient's sight.

To recover vision, opacification of crystalline lens must be removed surgically because so far, there has not been found any method to recover its transparency. Removing the opaque cataract lens is made through a new technique in ophthalmological surgery, namely through phacoemulsification.

Removing the natural opaque crystalline lens involves its replacement with an artificial one. This procedure can affect the endo-ocular structures and specifically the cornea (endothelial cell layer).

Cataract surgery dates back about 300 years. If at the very beginning, the extraction technique was extracapsular, it has been abandoned because of frequent complications, respectively phototoxic and phacoanaphylactic uveitis. For about 80 years, cataract lens extraction has been performed intracapsularly. Extracapsular extraction has started to be used again, and today, phacoemulsification technique tends to become an ideal vision rehabilitation technique with a view to ensuring patients' quality of life.

Corneal transparency is controlled by an active endothelial ion pump that preserves a low level of hydration of the corneal stroma. When endothelial cells fall below 600-800 cells/mm^2, corneal decompensation and corneal edema occur as a result of ion pump damage.

Purpose of the paper

The aim of this study is to show the effects of cataract surgery by phacoemulsification on corneal endothelium, namely on the endothelial cell morphology and density, as well as the effect of those changes on the thickness and finally, on the corneal transparency.

I studied the factors that can lead to the loss of corneal endothelial cells, such as the amount of fluid used during surgery, the total amount of ultrasound, cumulative dissipated energy (CDE) and endothelial cell loss in emmetropic, myopic and hyperopic patients. Endothelial cell morphology is very important, so I studied the morphology of these endothelial cells, respectively that the disruption of hexagonality can lead to endothelial decompensation. I studied the way endothelial dystrophy reacts to surgical trauma.

Providing corneal transparency is the main purpose of the ophthalmic surgeon. Loss of corneal transparency is considered a surgical failure with repercussions on the quality of life and even on surgeon.

Materials and methods

The study was conducted in the Ophthalmology Clinical Department within the Clinical County Hospital of Sibiu and at the level of the Ocular Surface Research Centre of the Faculty of Medicine, “Lucian Blaga” University of Sibiu, on a group of 317 eyes from 298 patients, 38 patients being operated on both eyes, patients who were operated for cataract through the phacoemulsification method.

The study was conducted over a period of 3 years, selecting the cases included in the study. Data were collected during surgery noting down phacoemulsification

time, the amount of ultrasound, CDE and the amount of fluid used. Measuring endothelial cells and cornea thickness was made with specular microscope.

Inclusion criteria for patients:

1. Patients' age: 45-95 years old;
2. Age-related cataracts, with a degree of sclerosis of the nucleus between 1 to 3;
3. Surgeries performed by the same surgeon;
4. Same surgical technique.

Exclusion criteria:

1. Pathological cataracts of local (ocular) cause or general (systemic);
2. Pachymetry greater than 0.70 mm ;
3. Number of endothelial cells less than 1200

The study group was selected from patients operated for cataract during January 2012 - January 2015, according to the above-mentioned criteria.

Pachymetry involves measuring corneal integrity. Normal thickness in the central region of the cornea is 0.49 to 0.56 mm. Normal endothelial cell density is 1800-2500 cells / mm^2. Pachymetry was performed by specular microscopy.

Specular microscopy

Endothelial cell density and morphology was studied using specular microscopy. I used CSO SP 01 specular microscope that allows obtaining electronic images of corneal endothelium without any contact between the device and the patient.

Pachymetry and endothelial cell count was done in the days before the surgery and 7-14 days later.

Biometry was made by Ultrascan ultrasound (Figure no. 5) after performing kerato-refractometry with Shin Nipon auto kerato-refractometer (Figure no. 6).

Surgical technique

All surgeries were performed by the same surgeon using the same surgical technique and using the Infinity® phacoemulsification device.

The time of surgery was decided by the effect cataract has on the patient's visual acuity, on the visual demands of patients. There was no standard criterion requiring the time of surgery. The decision was based on patient's whish. I believe that the decision for cataract surgery must belong to the patient, under the guidance of the ophthalmologist.

Preoperative preparation of the patient

Patients are hospitalized on the day of surgery or the day before with laboratory tests (ESR, CBC, glucose, urea, creatinine, APTT, INR, urine analysis test) already performed. I also asked for a clinical internal or general examination and according to the associated pathology of the patient, I required other tests, as well. The current trend is for outpatient cataract surgery. The progress made in recent years through very small incisions without sutures and the topical anesthesia allow the immediate postoperative recovery of the patient.

Phacoemulsification is the most used procedure in cataract surgery. The operation is performed under a microscope and does not require sutures. There are practiced incisions less than 3 mm and then, with a help of a probe that uses ultrasonic vibration triturating the crystalline lens, afterwards aspirating the contents of the crystalline lens. Once the crystalline lens has been removed, an artificial lens with patient's specific characteristics is placed instead of the natural one.

In recent years, a special laser, the femtosecond laser, executes a part of the cataract surgery, about 50%, without the need to use knives and forceps.

Preoperatively, eyelid toilet by washing with soap and water was performed, as well betadine 1% skin disinfection. We sedated the patient with a tablet of algocalmin and dormicum. Anesthesia was topical using forte tetravisc, one drop in the supine position, directly into the cornea, about a half hour before surgery.

After the patient is brought to the operating room, on the operating table betadine 1% skin disinfection is once again performed and one drop of betadine 0.5% is administered in the upper and lower conjunctival sac.

Mydriasis was carried out by the administration of parasympatholytic (mydrum, tropicamide) and sympathomimetics (neosinefrin, fenefrin) and a NSAID in order to potentiate the mydriatic effect. For infection prophylaxis, a broad-spectrum antibiotic eyewash was administered.

Phacoemulsification stages – technique used in the current stage

Mydriasis Preoperative mydriasis was performed by pupil dilation with Mydrum Tropicamide and Neosinefrin or Fenefrin administered 2-3 times in instillations, one hour before surgery.

Local-Topical anaesthesia with TetraViscForte administered half an hour before surgery.

Blepharostat. It is applied to remove eyelids. There has been used a blepharostat that does not put pressure on the eyeball.

For the success of surgery, and given the fact that topical anesthesia is involved, we must accomplish a very good cooperation between the patient and surgeon. Therefore, the patient is asked to look upwards and not to move his eyeballs.

Incision. I practiced two incisions (port site) at around 3 and 9 o'clock positions, of 1.2 mm by which the chopper and the irrigation-suction system were inserted. At 12 o'clock position or less right laterally, a 2.2 mm incision was practiced to insert the phacoemulsification probe. The incision practiced is a stepped incision into clear cornea.

The injection of viscoelastic substances

In order to preserve the anterior chamber, a viscoelastic substance is inserted here, a substance that protects corneal endothelium. The substance used in all cases was Viscoat, which is a dispersive viscoelastic substance. If it is a very elastic capsule, after Viscoat, Provisc is also inserted in the anterior chamber to prevent capsulorhexis skidding.

For advanced cataracts without red pupillary reflex, before inserting the viscoelastic substance, colour agent (trypan blue) was introduced into the anterior chamber under air protection to **colour the anterior capsule,** so as to be able to be viewed in capsulorhexis vision.

Capsulorhexis. Capsulorhexis or anterior capsulotomy firstly begun with the needle, then it continued with the forceps, aiming at a continuous round capsulorhexis.

Femtosecond laser, which is the latest technology in cataract surgery, accomplishes a continuous and centred capsulorhexis.

Liquefracture i.e. liquid separation of cortex from the capsule and nucleus hydrodelineation, that is nucleus separation from the cortex. This was performed with a special cannula, namely liquefracture cannula.

Phacoemulsification

In all cases, phacoemulsification was performed with the Infinity device.

The technique used was “divide and conquer” in order to divide the nucleus into two parts through sculpting, then stop and chop through the chopping method. Epinucleus is aspirated in the epy mode. Cortical remnants were sucked through the technique of bimanual irrigation-aspiration. Sometimes, posterior capsule polishing was needed through the polish mode.

Integral capsular bag is filled with cohesive viscoelastic substance (Provisc) or methylcellulose.

Artificial lens implantation

In all cases, foldable artificial lens was implanted, injected into the capsular bag with a special device for each type of lens.

After placing the lens, the entire viscoelastic substance from the anterior chamber and capsular bag under the pseudofak is removed by irrigation-suction. All viscoelastic substance must be removed, otherwise intraocular pressure can increase.

All three incisions are hydrated in order to achieve hydro-sealing, hydro-suture of the wounds, with a view to rebuild the anterior chamber and the eyeball tone.

Broad-spectrum antibiotic eyewash is administered, as well as an ointment and occlusive dressing for 24 hours.

Postoperatively, depending on the wish and ability of patient, he/she was hospitalized overnight or not.

Postoperative treatment consisted of antibiotic eyewash and anti-inflammatory steroid and ointment use at bedtime.

Check-up was mandatory one week postoperatively.

2-3 weeks later, after ending the antibiotic eyewash and the anti-inflammatory steroid, a non-steroidal anti-inflammatory eye drops are administered for 3-4 weeks more.

Results and discussions

I have structured the study results on different criteria developing the following sub-sections:

1. Endothelial cell loss after phacoemulsification of crystalline lens opacification.
2. Changing cornea thickness.
3. Loss of endothelial cells during phacoemulsification related to the amount of fluid used.
4. Loss of endothelial cells in relation to phacoemulsification time.
5. Endothelial cells loss according to the CDE used.
6. Endothelial cell loss in myopic patients.
7. Endothelial cell loss in hyperopic patients.
8. Endothelial cell loss in emmetropic patients.
9. Changes in the morphology of endothelial cells.
10. Endothelial dystrophy - risk factor for cataract surgery by phacoemulsification.

1. Endothelial cell loss after phacoemulsification of opaque crystalline lens

Endothelial cell analysis was done for each patient individually, studying the pre and postoperative cell density. I studied endothelial cell loss in the right eye and left eye in the study group (Figure no. 1).

The average rate of endothelial cell loss for the right eye (RE) was 450.78 and for the left eye (LE): 415.89 and 433.62 for both eyes (Figure no. 2).

Of the total number of cases for statistical processing, there were eliminated the cases with possible errors of measurement.

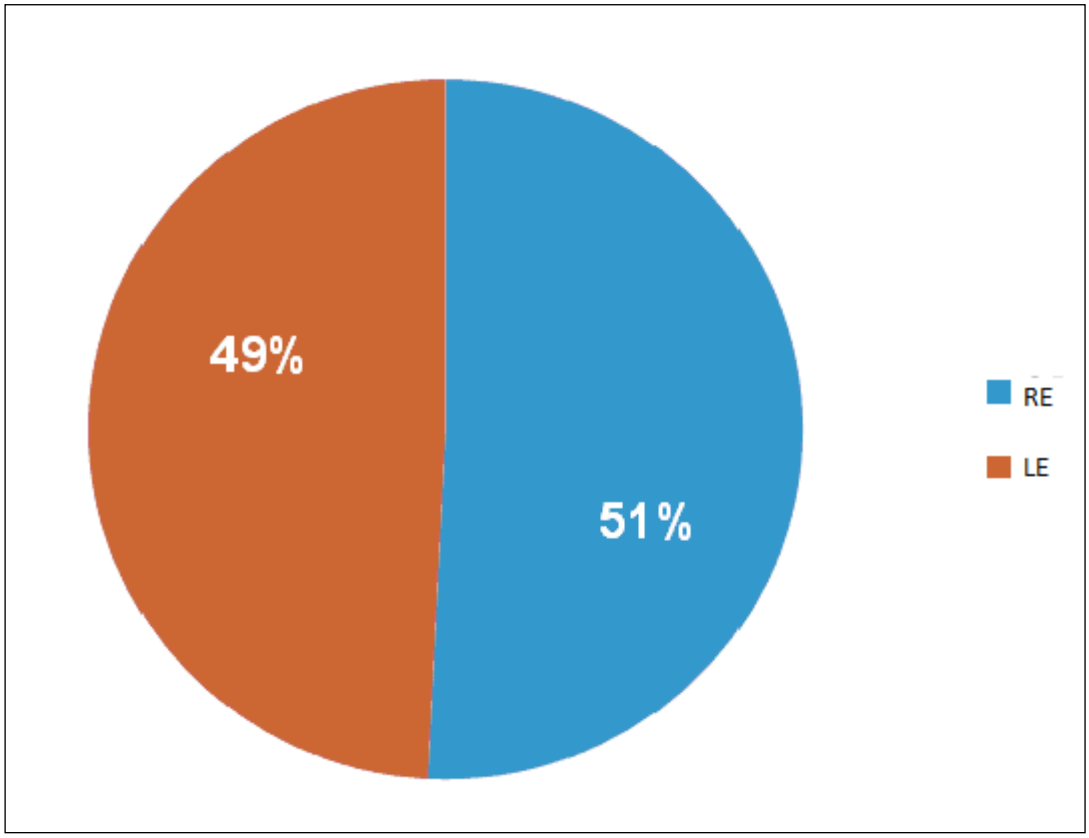

Figure no. 1. Eyes distribution

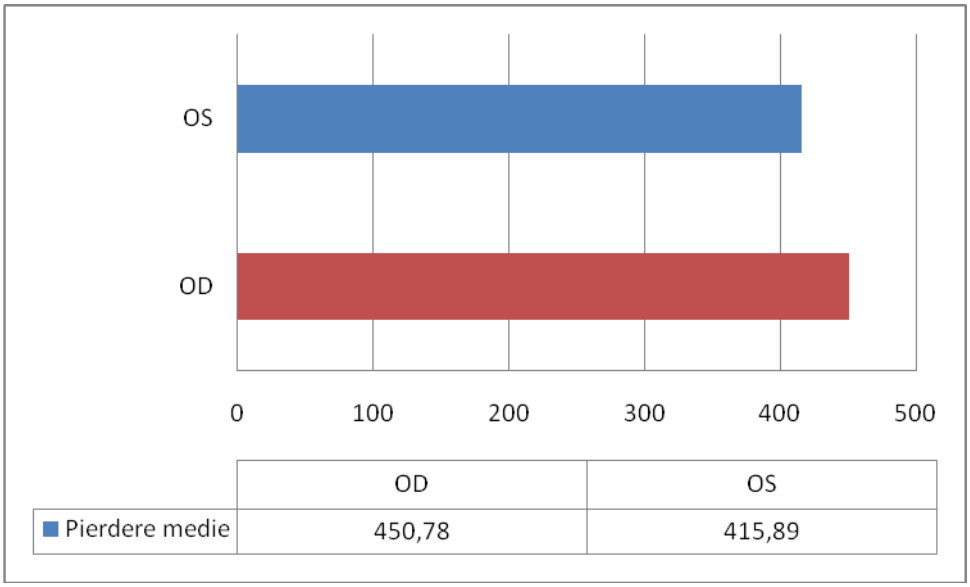

Figure no. 2. Average cell loss per eyes

2. Changing corneal thickness

After cataract surgery by phacoemulsification corneal thickness changes, meaning it increases due corneal hydration during surgery.

I studied this thickness increase of the cornea and I obtained the following data: in the right eye, thickness difference is of 30.67 microns and in the left eye, the difference is of 34.95 microns (figure no. 3).

It has been found that corneal thickness increase was made proportionally with the loss of endothelial cells.

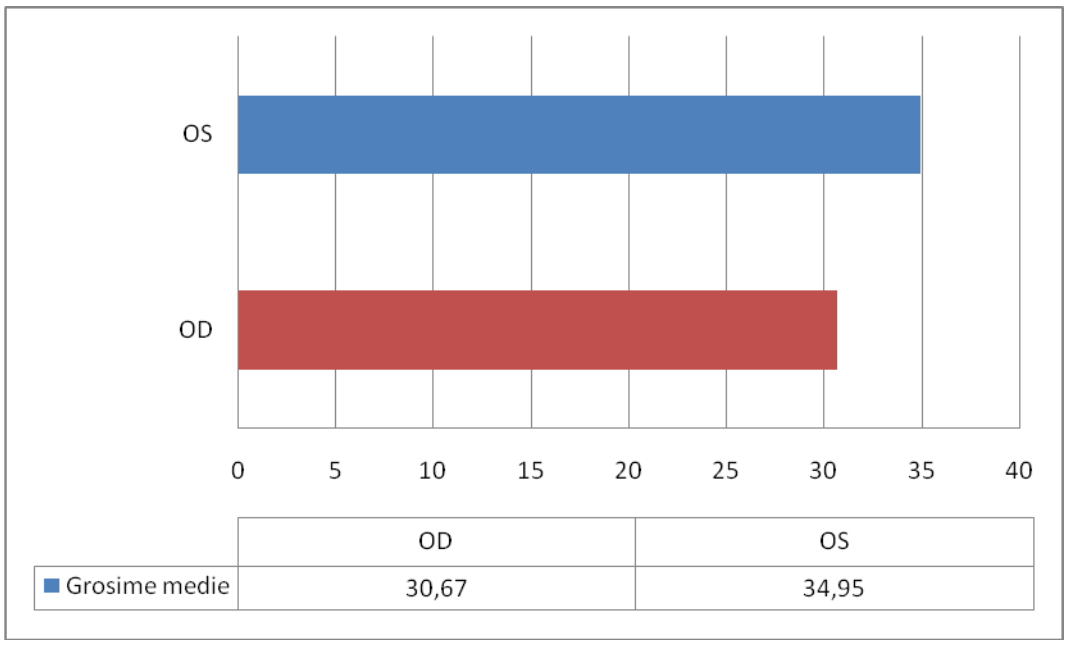

Figure no. 3. Average rate of corneal thickness increase

3. Loss of endothelial cells during phacoemulsification related to the amount of fluid used

The irrigation fluid used in all cases was the BSS solution. At the end of each operation, I measured the amount of fluid used and correlated it with the loss of endothelial cells (Figure no. 4). Data were statistically analyzed.

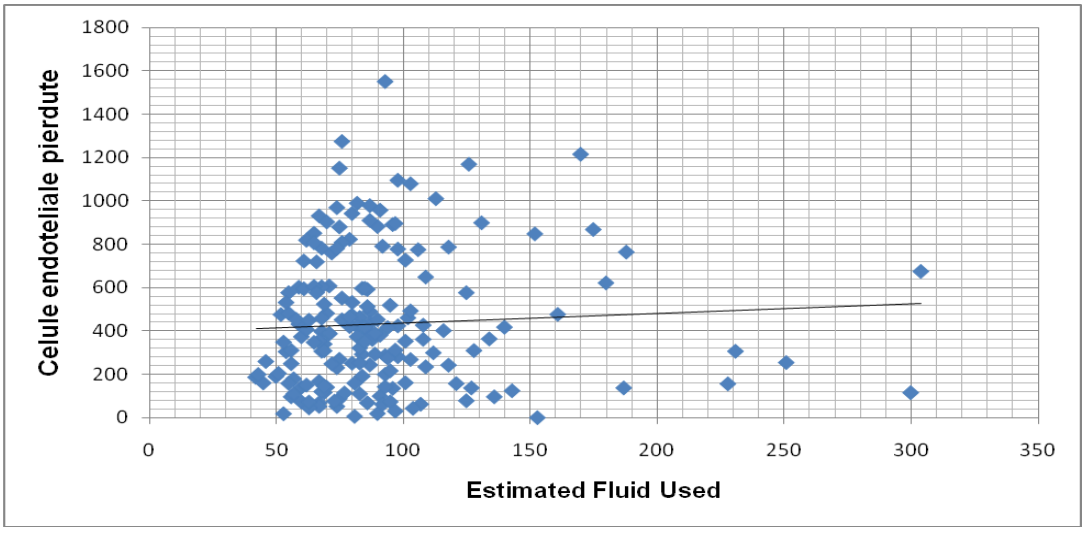

Figure no. 4. Estimated fluid used

Statistical analysis shows a poor correlation between the quantity of fluid used and the number of endothelial cells lost.

4. Loss of endothelial cells in relation to the ultrasound total time

Ultrasound total time was measured at the end of each surgery and there have been reported the number of lost endothelial cells (Figure no. 5). Data were statistically analyzed.

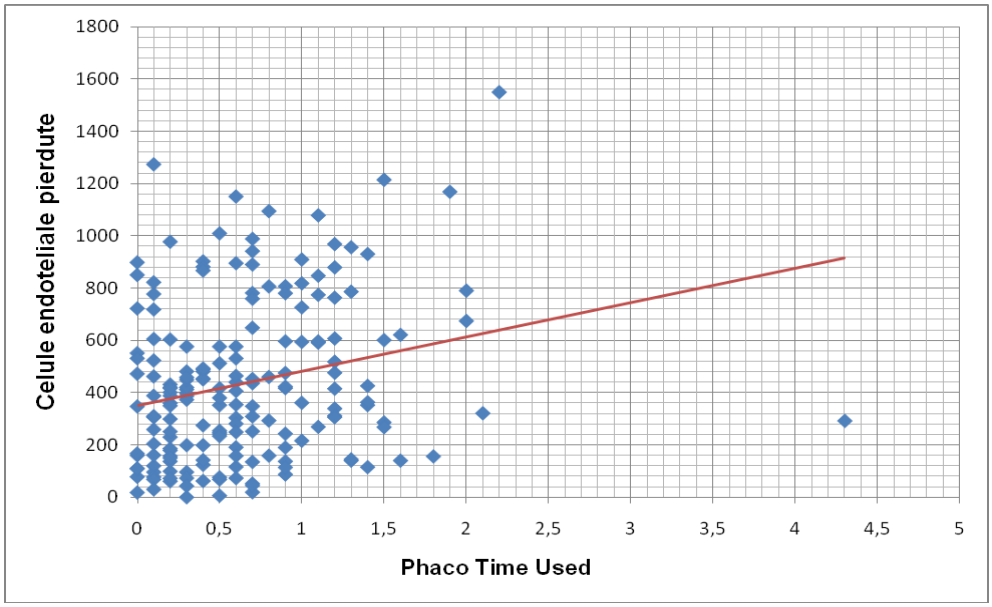

Figure no. 5. Phaco time used

`Statistical analysis shows a slight correlation between the total time of ultrasound and the number of lost endothelial cells.

5. Loss of endothelial cells according to the CDE used

Cumulative dissipated energy (CDE) was measured during every surgery and there was reported the number of lost endothelial cells (Figure no. 6). The data were statistically analyzed and the following results were obtained:

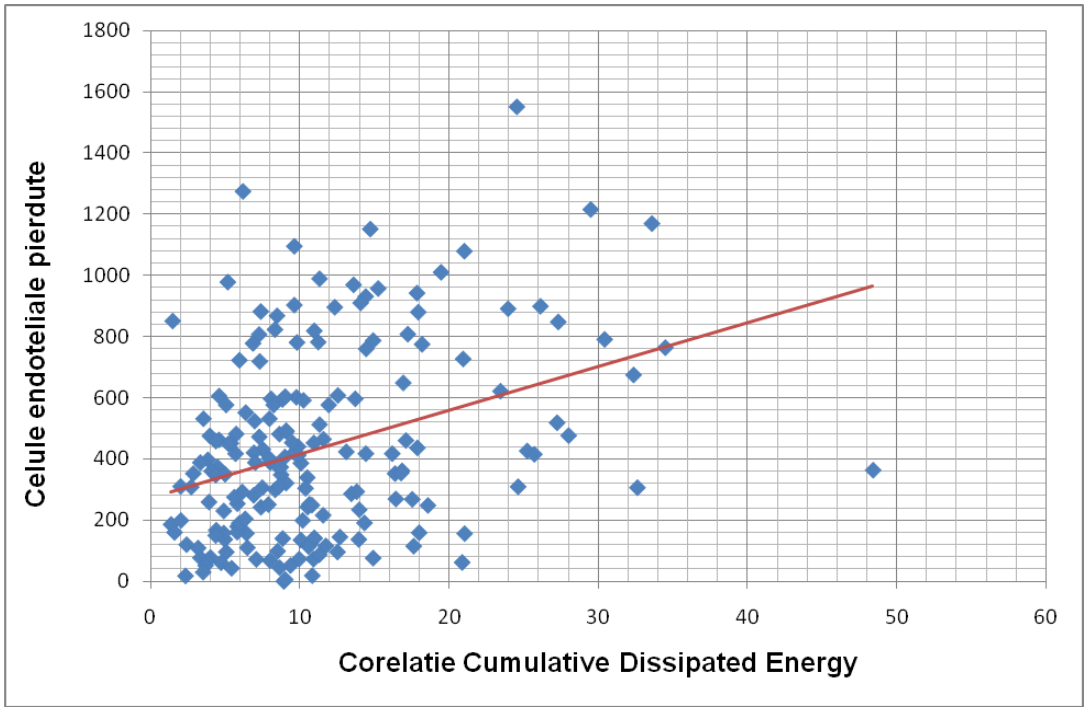

Figure no. 6. Cumulative Dissipated Energy correlation

The statistical analysis shows a strong correlation between the CDE and the number of lost endothelial cells.

6. Endothelial cell loss in myopic eyes

I considered it is important to study the rate of endothelial cell loss in myopic eyes. Myopic patients can sometimes be very happy after the cataract surgery; by removing the crystalline lens the patient may become emmetropic and can give up wearing glasses, which he/she has been done for the entire life. Cataract surgery in myopic patients is a real lens refractive surgery. The implant can correct any degree of myopia, even astigmatism by implanting a toric artificial lens.

In myopic eyes, extra precautions must be taken. Preoperatively, a detailed examination of the retina should be carried out in order to reveal any retinal cracks, central of peripheral chorioretinal degeneration, epiretinal membrane. These have to be identified and explained to the patient because they can negatively influence the postoperative outcome and the patient's dissatisfaction. If the patient has been informed before the operation, the surgeon's displeasure is diminished.

Biometrics can be easily mistaken because of the posterior staphyloma and postoperatively, hyperopia can result, which is very unpleasant for the patient. From the study, I observed that some myopic patients wish to remain myopic, but at a lower grade, of 2-4 dioptres. Preoperatively, I discussed with the patients and I have explained all variants to them.

Postoperatively, these patients should be monitored carefully because they show a high degree of retinal complications. Although they became hyperopic, they should continue to be followed-up, as retina remained with the same possible complications.

In this study, of 185 selected eyes, 27 representing 15% were myopic. CDE influence was statistically analyzed on the loss of endothelial cells, as follows (figure no. 7):

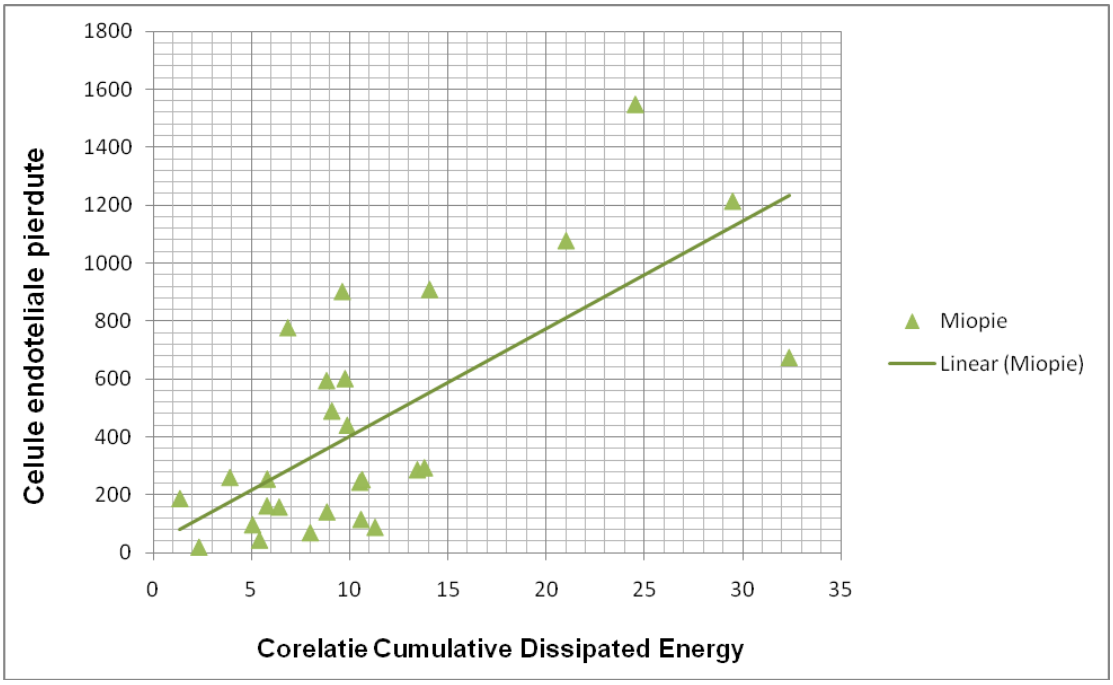

Figure no. 7. Cumulative Dissipated Energy - correlation

The statistical analysis shows a strong correlation between the CDE and the number of lost endothelial cells.

7. Loss of endothelial cells in hyperopic patients

Hyperopic patients represent a challenge during phacoemulsification surgery, especially because they have shorter eyeball and lower anterior chamber depth. A

small anterior chamber depth is associated with an overall decrease in the safety area, which can lead to difficulties in achieving corneal incisions, capsulorhexis and endothelial complications.

Pre-existing hyperopia may change the intraoperative course and the postoperative cataract development. Endothelial cell loss may be higher after surgical trauma, therefore corneal endothelium must be extra protected with viscoelastic substances.

Phacoemulsification surgery in the presence of hyperopia requires more attention. Biometrics and specular microscopy are very important in preoperative preparation of the patient. Hyperopic patients are a happy group of patients, being no longer dependent on the heavy and uncomfortable glasses after surgery.

There were 83 hyperopic patients, in whom CDE was correlated with the loss of endothelial cells (figure no. 8).

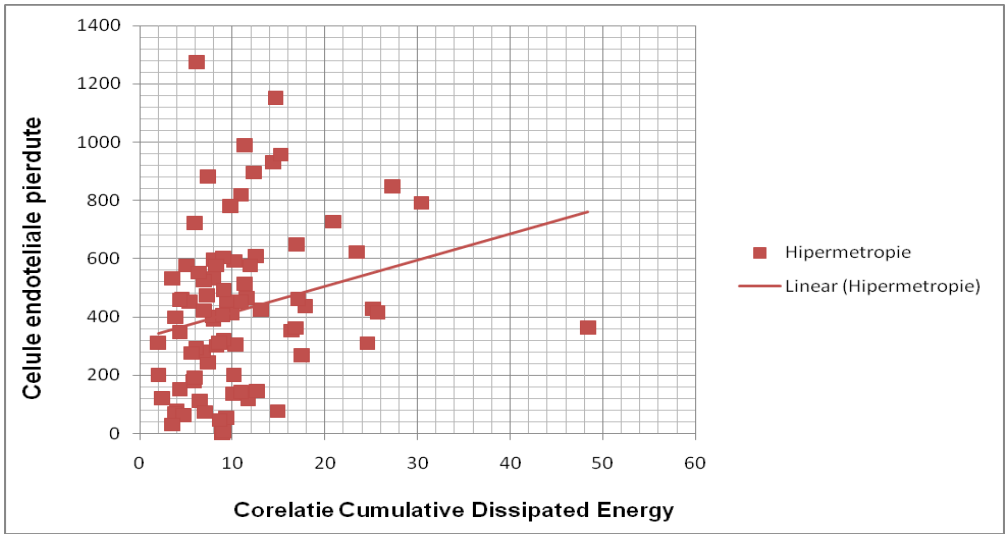

Figure no. 8. Cumulative Dissipated Energy - correlation

The statistical analysis shows a slight correlation between the CDE and the number of lost endothelial cells.

8. Loss of endothelial cells in emmetropic patients

It is assumed that emmetropic eyes behave normally to the surgical trauma.

Regarding the study group, there were 75 emmetropic patients, in whom CDE was correlated with the loss of endothelial cells (Figure no. 9).

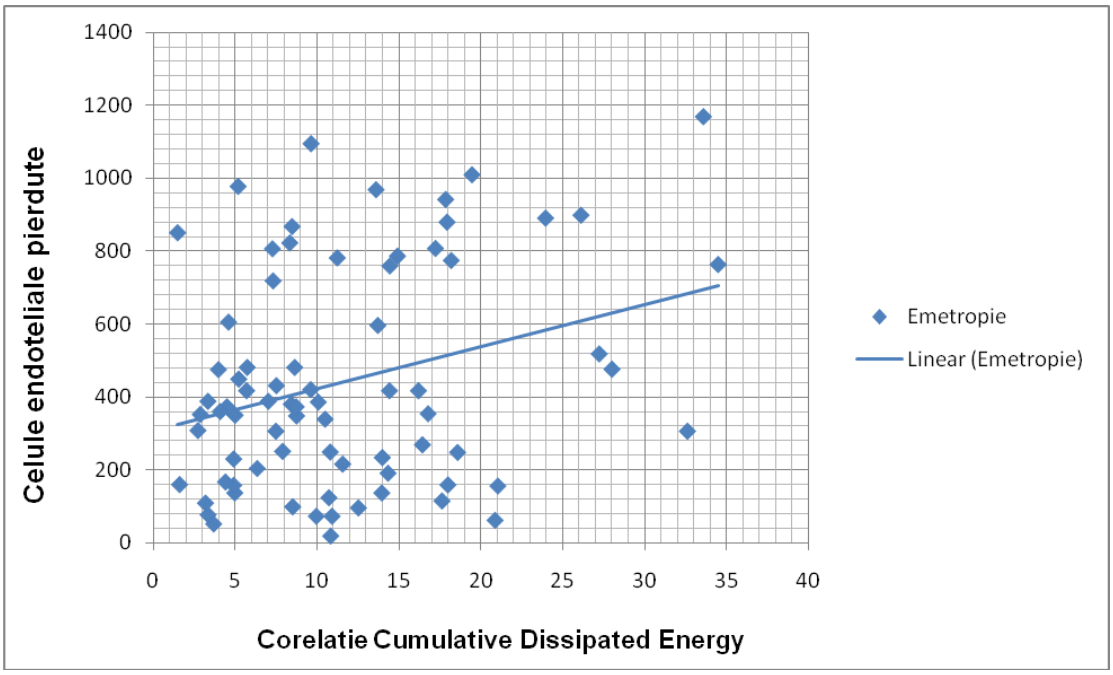

Figure no. 9. Cumulative Dissipated Energy - correlation

Statistical analysis shows a slight correlation between the CDE and the number of lost endothelial cells.

Comparative analysis

I compared the endothelial cell loss in emmetropic eyes with myopic and hyperopic eyes (figures no. 10,11,12).

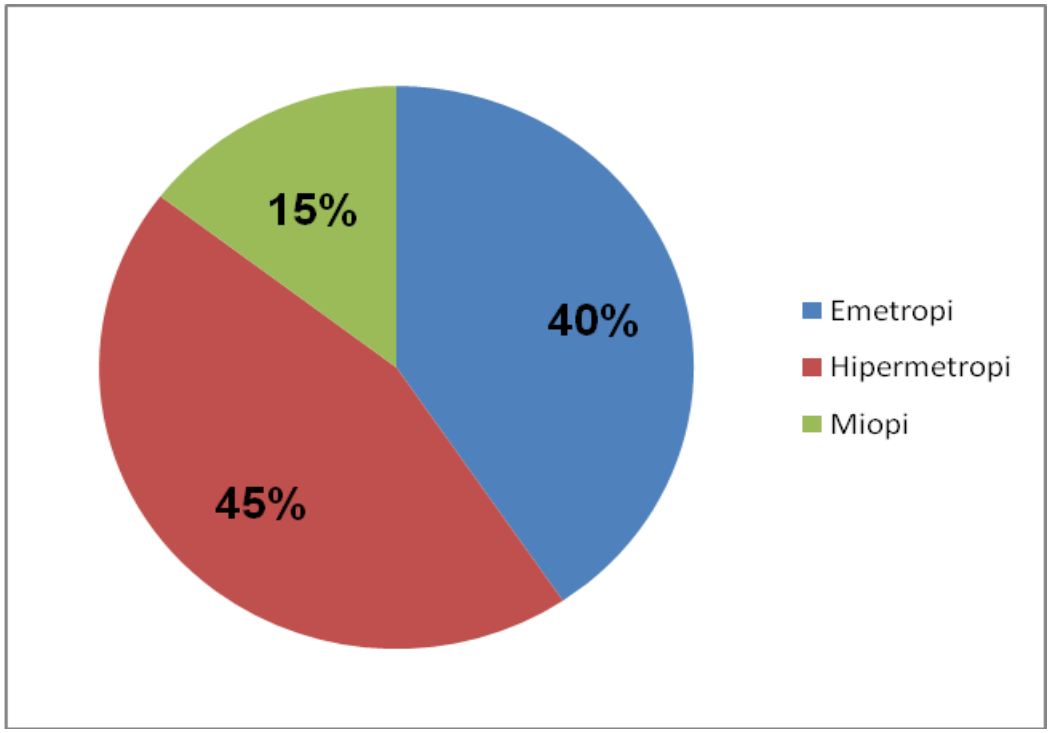

Figure no. 10. Comparative analysis of endothelial cells loss

9. Changing endothelial cells morphology

Endothelial cell layer is a single hexagonal layer of cells, very tightly linked to one another. This architecture is mandatory to be able to perform the main role to maintain the integrity of the cornea. There are 3000-4000cells./mm2, then their number decreases in the second decade of life until 2500-2700 / mm2 in the eighth decade.

The loss of these cells is covered by neighbouring cell expansion to cover the gaps.

The hexagonal shape of these cells is essential to maintain the integrity of the cornea.

During phacoemulsification, these cells may lose this hexagonal character, which can lead to endothelial decompensation.

I selected 40 patients of the total study group, in whom I studied the change of the percentage of hexagonal cells.

Thus, the percentage of pre-operative hexagonal cells was of 40-60% with a mean of 51.2% and postoperatively, it was of 24-61% with a mean of 47.5%. Hexagonality loss rate was only of 3.7%

The loss of endothelial cell morphology was not significant; in the studied cases, there was no endothelial decompensation.

Postoperative corneal edema occurred in cases with higher loss of percentage of hexagonal cells, but it disappeared within 2-3 days.

Hexagonality is lost proportionally with the number of lost cells and with the increase of cornea thickness (figure no. 13), where there has been lost a large number of cells, 903 cells/mmm^2, corneal thickness significantly increased to 430 microns and lost hexagonality was of 21%.

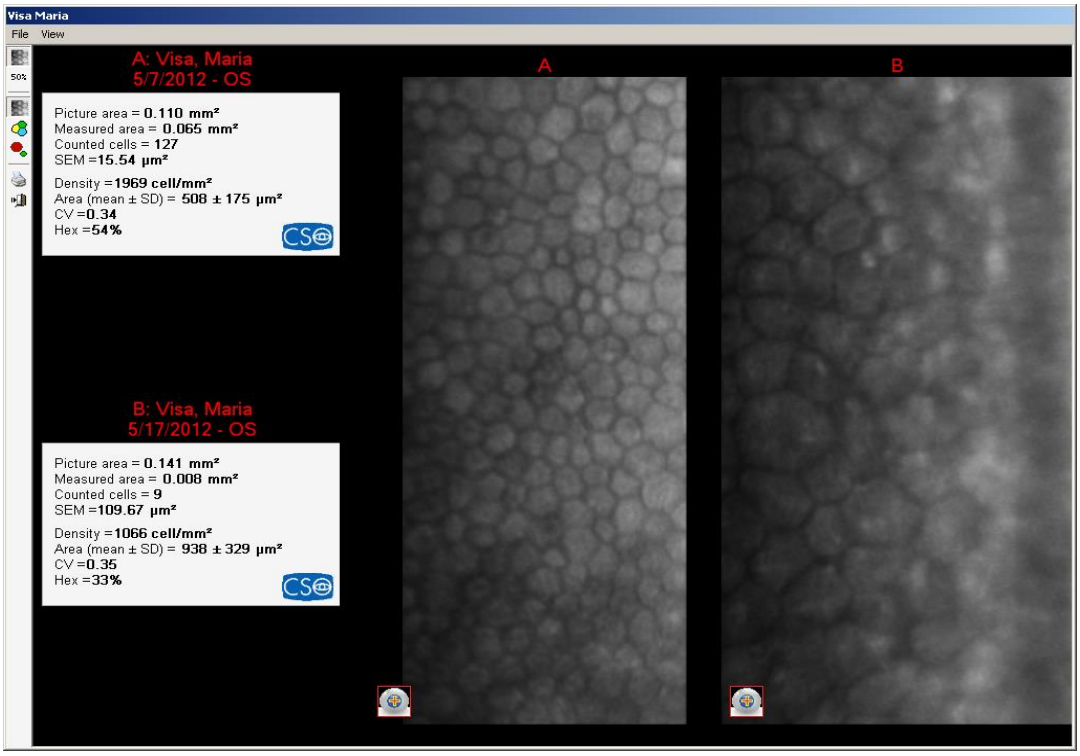

Figure no. 13. Cornea thickness

10. Endothelial dystrophy - risk factor for cataract surgery by phacoemulsification

Corneal endothelial dystrophy, cornea guttata and Fuchs endothelial dystrophy are corneal endothelial disorders, which if unrecognized or ignored preoperatively can lead to corneal decompensation with the emergence of highly unpleasant complications, namely bullous keratopathy.

Cornea guttata is an accumulation of collagen on the posterior side of the Descemet's membrane. It is probably secreted by the abnormal endothelial cells and may occur as a result to the old age.

Fuchs endothelial dystrophy is characterized by corneal swelling. When corneal edema is missing and only gout is present, this condition is called guttate cornea. Only confocal microscopy can distinguish between Fuchs endothelial dystrophy and cornea guttata. Specular microscope cannot detect the endothelium in the presence of corneal edema.

I studied the impact of phacoemulsification on corneal endothelium in the patients with endothelial dystrophy

Studying the pre- and postoperative corneal endothelial appearance, I found that in these cases, corneal decompensation that did not happen. Specular microscopy detects this corneal condition preoperatively, and I took all additional measures, such as excessive use of viscoelastic substances, sodium hyaluronate, reduced ultrasound time, and performing phacoemulsification in the capsular bag. Endothelial dystrophy, which is preoperatively known and treated appropriately can be stopped.

When corneal edema occurs, cataract surgery also requires corneal endothelial transplantation. Preoperative specular microscopy is mandatory. The use of cohesive and dispersive viscoelastic substances is necessary.

Of the studied cases, there have been found a number of 35 cases of cornea guttata (figure no. 14), who underwent cataract surgery. Being diagnosed preoperatively, I took every precaution and corneal decompensation has never occurred. There was no Fuchs endothelial dystrophy.

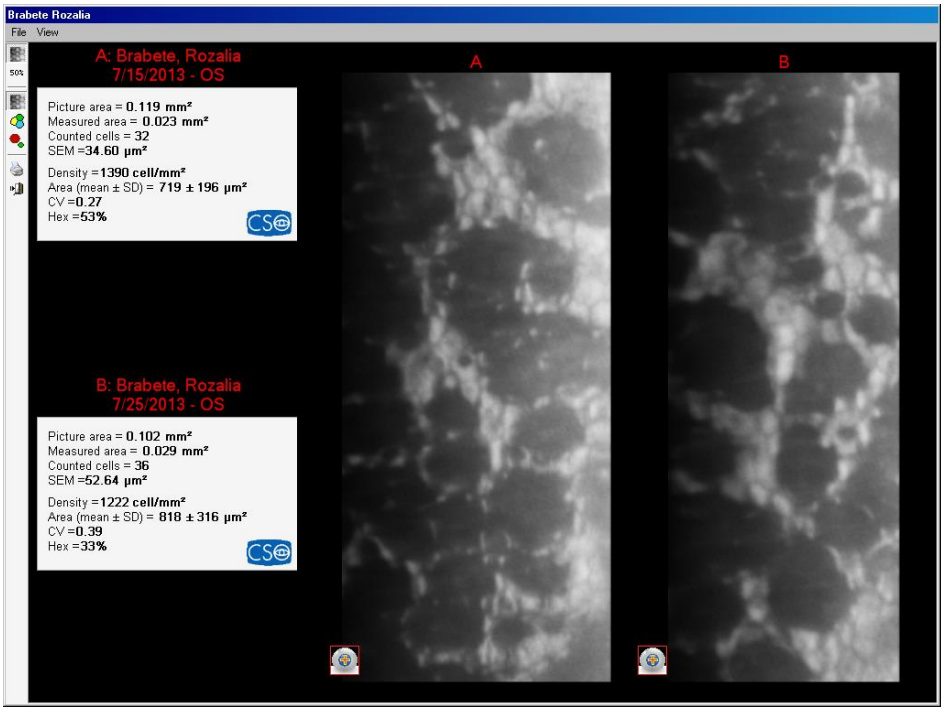

Figure no. 14. Cornea guttata

Literature gives similar data regarding the loss of endothelial cells loss through phacoemulsification. Therefore, a study in India shows that there is no difference to the loss of endothelial cells in the group in which ophthalmic viscoelastic devices (OVD) were used as against the group that used continuous irrigation of the anterior chamber.

Another study shows that use of OVD is essential for good postoperative results.

Cataract surgery is one of the most effective refractive surgeries. The new implant can correct any degree of myopic or hyperopic defect, even astigmatism during the surgery.

In our study, results were good, no patients presented complications related to corneal decompensation, such as chronic corneal edema or chronic edemato-bullous keratopathy.

We believe that the use of viscoelastic substances is essential for good postoperative outcomes.

Conclusions:

1. Phacoemulsification by microincisions is a very safe method to extract crystalline lens.
2. The use of viscoelastic substances is mandatory.
3. Gender distribution is not significant.
4. The average rate of endothelial cell loss was of 433.33 cells/ mm^2.
5. Corneal thickness increased by 32.81 microns on average.
6. Cornea thickness was increased proportionally with the loss of endothelial cells.
7. Endothelial cell loss is not related to age, but older people have fewer endothelial cells, so for the same number of lost cell, corneal decompensation occurs more often in older people.
8. Statistical analysis on the amount of liquid (BSS) used during surgery and the loss of endothelial cells shows a weak correlation, which is statistically insignificant.
9. There is a slight correlation between ultrasound total time used and endothelial cell loss.
10. There is a strong correlation between cumulative dissipated energy (CDE) and endothelial cell loss.
11. Regarding vices of refraction, endothelial cell loss was of 457 cells/mm^2 in emmetropic patients, 441cells/mm^2 in myopic patients and 421 cells/mm^2 in hyperopic patients.
12. In the study group, hexagonality of endothelial cells was lost in a percentage of 3,7%.

13. I studied 35 eyes with cornea guttata, in whom I applied intraoperative precautions, thus avoiding endothelial decompensation.
14. It is important to recognize corneal guttata, so specular microscopy is mandatory before surgery.
15. Phacoemulsification performed by an experienced surgeon, with modern equipment, as well as the use of new techniques and viscoelastic substances can lead to very good postoperative outcomes.
16. Nowadays, cataract surgery entirely rehabilitates vision, thus leading to increasing the quality of life of patients and ophthalmologist's consideration.

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