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Rīga Stradiņš University

Juris Vanags

Changes to the Anterior Capsular Opening of Human Lens after Cataract Surgery in Patients with Subluxated Lenses

Summary of the Doctoral Thesis
for obtaining a doctoral degree (*Ph.D.*)

Sector – Clinical Medicine
Sub-sector – Ophthalmology

Riga, 2021

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Content

Abbreviations

BCVA	Best Corrected Visual Acuity
CTR	Capsular Tension Ring
DALK	Deep Anterior Lamellar Keratoplasty
IL	Interleukin
IOL	Intraocular Lens
IQR	Interquartile Range
MCP1	Monocyte Chemoattractant Protein1
mCTR	Modified Capsular Tension Ring (Cionni)
MMP	Matrix Metalloproteinases
MS	Marfan Syndrome
LEC	Lens Epithelial Cells
Nd:YAG	Neodymium-doped Yttrium Aluminium Garnet
n.s.	Not Statistically Significant
PEX syndrome	Pseudoexfoliation Syndrome
P. Stradiņš CUH	Pauls Stradiņš Clinical University Hospital
TGF	Transforming Growth Factor
TGFβ2	Transforming Growth Factor Beta 2
VEGF	Vascular Endothelial Growth Factor

Introduction

Place of work

Pauls Stradiņš Clinical University Hospital (P. Stradiņš CUH), Eye Diseases Clinic, Department of Ophthalmology at Rīga Stradiņš University.

Importance of the Thesis

The prevalence of lens subluxation in a case of congenital pathology is about 6.4 cases per 100,000 people (Fuchs & Rosenberg, 1998), but where there are other grounds, including weakness in zonules associated with Pseudoexfoliation (PEX) syndrome or trauma, the frequency varies from 0.7 % of patients, and those for whom cataract surgery has been carried out (Tribus et al., 2007), up to 0.94 % (Celik et al., 2015). Taking into account the gradual increase in average life expectancy in Latvia, which has increased by 5 years in the past 19 years (Centrālā Statistikas pārvalde, 2019), an increase can also be expected in the number of cases of lens subluxation, mainly at the expense of patients with PEX syndrome, as the frequency of PEX syndrome is increasing with the increase in the age of patients (Astrom & Linden, 2007).

Lens subluxation surgery is one of the most complex types of surgery on the anterior part of the eye, with a longer time of surgery being typical. Individualised surgical tactics are required with a large chance of them needing to be forcibly changed due to complicated events, an increased frequency of intraoperative and postoperative complications, and potentially worse postoperative results when compared to a general cataract operation (Bayraktar et al., 2001; Blecher & Kirk, 2008; Clark et al., 2011; Hoffman et al., 2013; Vasavada et al., 2012a). Even though the phacoemulsification method does not

differ in the sense of visual acuity and postoperative complications from other contemporary lens subluxation surgery methods (for example, pars plana lentectomy with scleral fixation of the intraocular lens (IOL)) (Thapa et al., 2016), it does include several advantages within it – more surgeons (cataract surgery) are familiar with the method, there is more phacoemulsification equipment, a shorter period for learning the method, simpler additional instruments and auxiliary devices (capsular and iris hooks, capsular tension rings (CTR) and segments), the use of which is consequently easier to learn, a shorter surgery time (Thapa et al., 2016), as well as lower surgical costs compared to other methods. The introduction of additional instruments and auxiliary devices should also be noted, starting from capsular tension rings which appeared in 1991 (Hara et al., 1991; Nagamoto & Bissen-Miyajima, 1994) until their evolution into the CTR concept which is used nowadays(Legler et al., 1993), design variations in 2007 (Henderson Ring) (Henderson & Kim, 2007), application of the modified CTR (Cionni Ring and mCTR) from 1998 (Cionni & Osher, 1998), improvement of the design associated with Malyugin in 2012 (Malyugin B, 2012), use of the iris retractors in lens subluxation surgery from 1997 (Novak, 1997) and its gradual development in subsequent decades (Yaguchi et al., 2011, 2019).

Anterior capsular opening reduction in patients with subluxated lenses or with weak zonules after cataract surgery with small initial capsulorrexis, and the effect of this indicator on post-surgical outcomes, has not been previously researched or has been looked at only partly.

Aim of the research

The aim of the study was to analyse changes in the anterior capsular (capsulorrexis) opening after cataract surgery for patients with subluxated

lenses and to prove their connection with zonular weakness/absence, as well as the effectiveness of the surgical method used.

Thesis tasks

1. To evaluate the dimensions of the anterior capsular opening during surgery and their changes at various stages of observation in their dynamics and dependance on various factors.
2. To create a post-surgical 3-month values prediction model for the capsulorrexis area.
3. To identify patient groups with subluxated lenses with a greater risk of post-surgical and late complications.
4. To identify the indirect parameters of possible weak zonule stages.
5. To evaluate the effectiveness of auxiliary devices for subluxated lens surgery and adapt them for use in Latvia, so that surgery for subluxated lens can be made similar to everyday cataract surgery, to the maximum degree.
6. To develop recommendations for surgical tactics for the treatment of subluxated lenses, as well as to reduce and solve the risks of post-surgical and late complications.

Hypotheses of the Thesis

1. The anterior capsular opening reduces rapidly in weakened or non-existing zonules.
2. The surgical auxiliary devices that are used assist in maintaining the long-term result for the existing zonules and the effective solution of later complications.

Scientific novelty

1. Statistically significant capsulorrexis reduction indicators were found in the work which allow for the prediction of the possible long-term results of the surgery.
2. The reduction field and the speed of reduction of the anterior capsular opening after cataract surgery for patients with subluxated lenses and their connection to various factors, were investigated.
3. The first results of late post-surgical complications after cataract surgery, for patients with subluxated lenses were obtained.
4. Additional data about the effectiveness of auxiliary devices used in cataract surgery for subluxated lenses were obtained.
5. The academic innovation has been confirmed in 5 international publications. The results of the work have been reported at 10 international and 5 local conferences.

1 Materials and methods

1.1 Characteristics of research sample

There were 53 patients included in the sample to be analysed. Patients were operated on from 1st January, 2011 to 31st December, 2015.

1.2 Research design

Prospectively, an observational survey at one centre on patients with clinically diagnosed subluxated lenses, defined as iridodonesis and phacodonesis, and/or clinically confirmed zonular absence.

Six months of active post-surgery observation was planned in the observational survey, with the collection and analysis of the data. The patient would be examined if there was a new complaint in the period after the 6-months period if later complications were identified after the surgery.

The survey was undertaken within the framework of the "Development of the Optimal Method for the Fixation of Dislocated Lenses" paper with the permission of the P. Stradiņš CUH Development Association's Clinical Research Ethics Committee (Resolution No. 080110-7L).

1.3 Patients, inclusion and exclusion criteria, and investigation

There were 130 patients consulted, with the diagnosis being subluxated lenses, in the period from 2011 to 2015. The initial diagnosis for these patients was determined: 1) by the treating eye doctor, 2) by an emergency ophthalmologist at the P. Stradiņš CUH Emergency Medical Centre, 3) by the operating surgeon during the primary consultation, 4) at the first examination by doctors of' patients who had arrived for the planned cataract surgery at an

ophthalmic day care unit. The criteria for sending the patient to the consultation were:

1. Clinically diagnosable iridodonesis;
2. Phacodonesis;
3. Zonular absence;
4. Another cataract surgeon's refusal to operate on a patient with a suspected subluxated lens.

Having undertaken examinations and consultations with 130 patients, 74 patients were selected for inclusion in the research, with the level of subluxation being determined by the Waisvol et al. classification (Waiswol & Kasahara, 2009), which also conforms with the Hoffman et al. classification (Hoffman et al., 2013). In the case of Grade I subluxation according to Waisvol, or minimal subluxation according to Hoffman, the lens is found ophthalmoscopically in the pupillar area with the edge of the lens not being visible, with only iridodonesis and phacodonesis able to be established, although there could also be an asymmetric and deep anterior chamber. In the case of Grade II (Waisvol) or moderate (Hoffman) subluxation, if the edge of the lens is visible in the pupillar area, the lens takes up at least 2/3 of the pupillar area. In the case of Grade III or serious subluxation, the lens takes up at least ½ of the pupillar area. In the case of Grade IV, the lens is completely dislocated and is not visible in the pupillar area, see Figure 1.1 below.

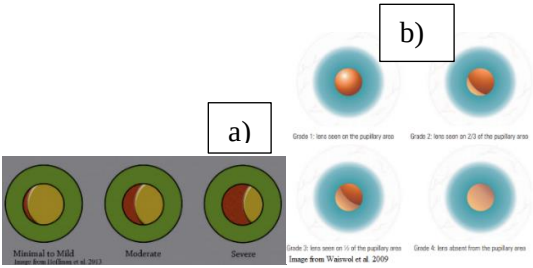


Figure 1.1 **Subluxation grade a) according to Hoffman, b) according to Waisvol**

Inclusion criteria:

1. Age of the patient > 18 years;
2. Phacodonesis;
3. Iridodonesis;
4. Lens subluxation of Grade I, II or III;
5. Deterioration in visual acuity, or lens opacification;
6. Adequate enlargement of the iris;
7. The patient has agreed to surgery and participation in the study.

Exclusion criteria:

1. Grade IV lens subluxation (dislocation in a vitreous body);
2. History of vitrectomy surgery;
3. Anterior capsular rupture during surgery;
4. Posterior capsular rupture during surgery;
5. Requirement of a vitrectomy during surgery;
6. Decompensated glaucoma, active iridocyclitis, retinal detachment, haemophthalmus, marked blepharitis, dacriocystitis;
7. The patient has not attended follow-up visits.

In the final analysis, 53 Patients were included.

Examinations were made on patients:

1. Standard ophthalmological history was collected;
2. Best corrected visual acuity (BCVA) with a *Snellena* equivalent table. Visual acuity was expressed in decimals;
3. Non-contact tonometry;
4. Biomicroscopy;
5. Biometry and keratometry and calculation of IOL with a Carl Zeiss IOL master (Carl Zeiss Meditec AG, Jena, Germany);
6. Ultrasound of the eye;
7. *Fundus oculi* examination;

8. Photo documentation of the anterior part of the eye with the pupil dilated to the maximum extent;
9. During the surgery – video registration of the surgical process.
10. The visits were grouped in the following way:

a. V0-first visit – prior to surgery;
b. V1 – 1 day after surgery;
c. V2 – 1 week after surgery;
d. V3 – 1 month after surgery;
e. V4 – 3 months after surgery;
f. V5 – 6 months after surgery.

1.4 Control group

There were 31 patients with a macular hole or an epiretinal membrane included in the control group, on whom a cataract surgery was done a month before a vitreoretinal surgery. An anterior capsular opening reduction analysis was undertaken with an analysis of the one-month results.

1.5 Surgery

1.5.1 Research patient surgery

Patients were operated on with both local sub-tenon anaesthesia, as well as general anaesthesia. All surgeries were undertaken by 1 surgeon (JV). During the surgery, a temporal incision (2.75 mm) was made in the main cornea tunnel, with a 1.2 mm nasal paracentesis and the anterior chamber was filled up with a viscoelastic substance to prevent deflation of the anterior chamber and so that the further stages of surgery could be undertaken. After the creation of an interior capsular opening (continuous capsulorrhexis), further paracenteses were undertaken at 1.30 pm, 4.30 pm, 7.30 pm and 10.30 pm,

through which iris (Figure 1.2 a) or capsular hooks (Figure 1.2 b) were introduced into the anterior chamber, securing the lens bag to the capsulorrhexis edge with them to ensure the stability of the lens bag/lens during the operation (Figure 1.3). Modified CTR (Cionni) (Figure 1.4 a) or a CTR (Figure 1.4 b) was implanted in the lens bag, after the stabilisation of the lens bag with hooks.

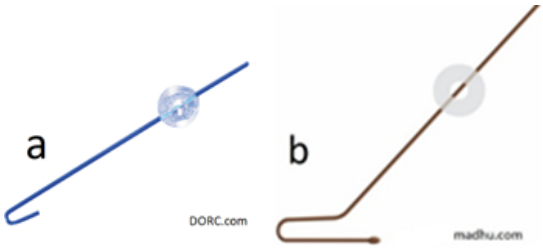


Figure 1.2 **Capsular bag attachment hooks a) iris retractors b) Mackool type capsular bag retractors**

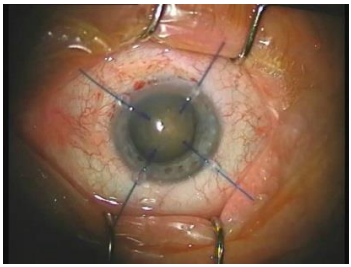


Figure 1.3 **Fixation of the lens bag with iris hooks**

If a Cionni ring was used, then immediately after its implantation, a scleral flap in *sulcus* area was created on the projection site and a sclerotomy or needle sclerotomy performed, through which the Cionni ring's fixation arm was attached with 10/0 polypropylene. A phacoemulsification of the nucleus of the lens was undertaken afterwards, and a manual irrigation-aspiration of the subcapsular layer was undertaken without an additional polishing of the lens

epithelial cells, and an IOL was also implanted. IOLs, which are similar in their technical specifications, were used and came from 3 manufacturers: Alcon [*Acrysof SN60AT, MN60 MA, IQ SN60 WF; Alcon Surgical, Inc., Fort Worth, Texas, USA*], AMO [*Tecnis ZCB00; Abbott Medical Optics Inc (now Johnson and Johnson), Santa Ana, California, USA*], and Medicontur [*877FABY; Medicontur Medical Engineering Ltd., Zsámbék, Hungary*]. After the placement of the IOL, the hooks securing the capsular bag were removed, the viscoelastic material was rinsed out and the wounds closed. The closest and most precise IOL calculation (measured with a dioptre) was chosen for the IOL's implantation, irrespective of the manufacturer, to ensure the best postoperative visual acuity.

If a CTR was implanted, the operating surgeon (JV) implanted Medicontur lenses more frequently, as they have double haptics, which provide additional fixation points for the possible repositioning of artificial lenses and fixation in the case of late dislocation. Small capsulorrhexis were not enlarged as this is a complex procedure which can cause additional zonular damage. After surgery, local therapy was prescribed for patients with antibiotics and drops containing dexamethasone, for one month.

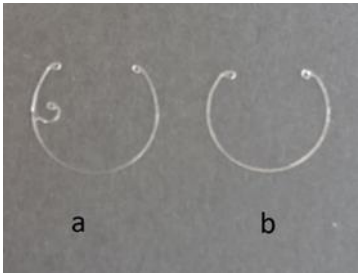


Figure 1.4 **a) mCTR (Cionni) b) CTR**

1.5.2 Control group patient surgery

Patients were operated on with local sub-tenon anaesthesia. All operations were conducted by one surgeon (JV). During the surgery, a temporal incision (2.75 mm) was made in the main cornea tunnel with a 1.2-mm nasal paracenteses as well, and the anterior chamber was filled up with a viscoelastic material, to prevent deflation of the anterior chamber and so that the further stages of surgery could be undertaken. After creation of an anterior capsular opening (continuous capsulorrhexis), a hydrodissection of the nucleus of the lens was undertaken. A phacoemulsification of the nucleus of the lens was undertaken afterwards, with a manual irrigation-aspiration of the subcapsular layer without an additional polishing of the lens epithelial cells, and an IOL also being implanted. IOLs, similar in their technical specifications from 3 manufacturers were used: Alcon [*Acrysof SN60AT, MN60 MA, IQ SN60 WF; Alcon Surgical, Inc., Fort Worth, Texas, USA*], AMO [*Tecnis ZCB00; Abbott Medical Optics Inc (now Johnson and Johnson), Santa Ana, California, USA*], and Medicontur [*877FABY; Medicontur Medical Engineering Ltd., Zsámbék, Hungary]* (Figure 1.5).

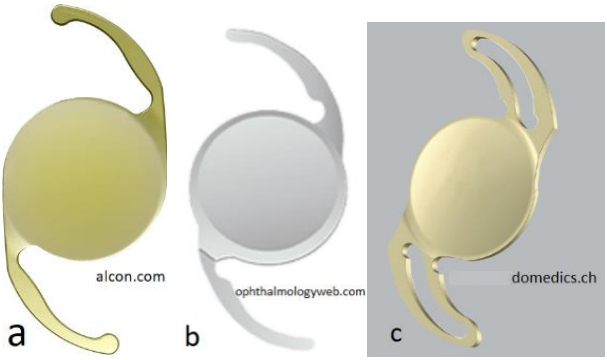


Figure 1.5 **IOL manufacturer a) Alcon SN60WF IOL, b) Tecnis ZCB00 IOL, c) Medicontur 877 FABY IOL**

After the IOL was implanted, the viscoelastic material was washed out and the wounds closed. The closest and most precise IOL calculation (measured with a dioptre) was chosen for the IOL implantation, irrespective of the manufacturer, to ensure the best postoperative visual acuity. After surgery, local therapy was prescribed for patients with antibiotics and drops containing dexamethasone, for one month.

1.6 Anterior capsular measurements

Photo documentation (Carl Zeiss Fundus Camera FF450plus, Visupac 4.3 software [*Carl Zeiss Meditec AG, Jena, Germany*]) (Figures 1.7 and 1.8) of the anterior part of the eye was undertaken for patients with the pupil medically expanded to the maximum extent during all visits. Video registration of surgery was also undertaken (Figure 1.6).

Figure 1.6 **MEDIALINK equipment**

The anterior capsular opening (capsulorrhexis) was measured using Fundus Camera software (Visupac 4.3) and subsequently manually recalculated to the real measurements, using the IOL optic size measurement (6 mm) as the

reference measurement. The size of the IOL's optical field was calculated using the formula

$$S = \pi r^2 \text{ (S = 3.14 × 3 × 3 = 28.26 mm}^2\text{)} \quad (1)$$

The following equation was used to calculate the anterior capsular opening:

A = 28.26

B = X

$$X = \frac{28.26 \times B}{A}, \quad (2)$$

where A is the IOL's size, and B – the size of the capsulorrhexis, and were obtained using measurements using the Fundus Camera's Visupac software, X – is the real size of the capsulorrhexis. If the IOL could not be clearly seen due to the poor expansion of the pupil, the interlimbal distance was used as the reference measurement.

Figure 1.7 **Fundus Camera**

Example of a patient with capsulorrhexis measurements in a Visupac 4.3 environment from the 1st post-operation day (V1) to the 6th month (V5), see Figure 1.8

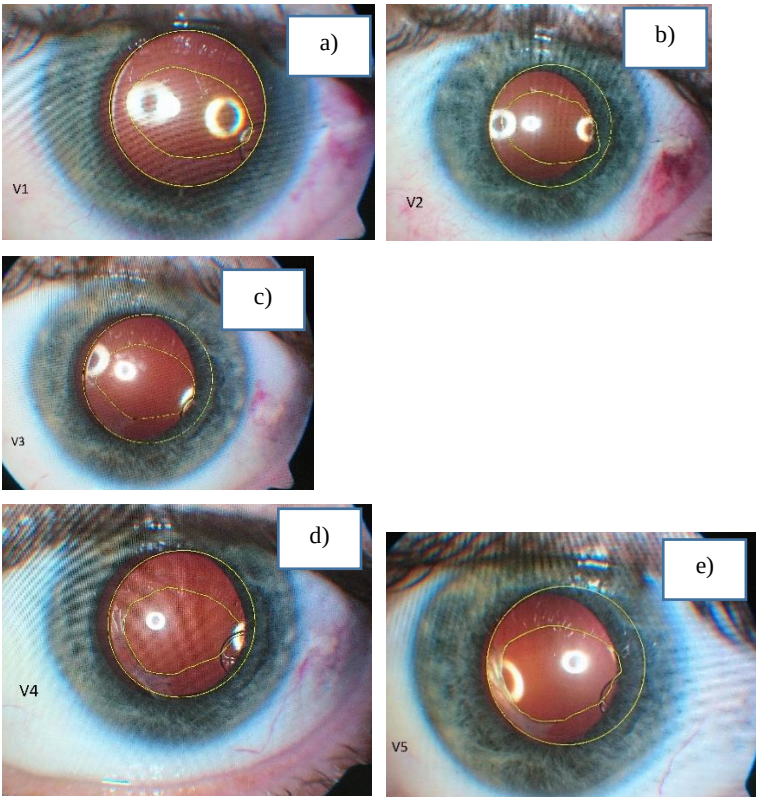


Figure 1.8 **Example of a patient with capsulorrhexis measurements: a) 1 day after surgery, b) 1 week after surgery, c) 1 month after surgery, d) 3 months after surgery, e) 6 months after surgery**

1.7 Statistical analysis

Normally distributed quantitative variables were described as a mean (M) and standard deviation (SD), or median (Md) and interquartile range intervals ([IQR]) as appropriate. Qualitative variables were expressed as a number (N) and a percentage ratio (%). The quantitative data for the two groups was analysed with a t-test or a Mann-Whitney test, while three and more groups were analysed using a dispersion analysis (ANOVA) or a Kruskal-Wallis test. A Spearman (rs) correlation coefficient was used to analyse correlations between continuous quantitative variables. The classification of the correlation strength according to the value of the correlation coefficient rs was as follows: rs = 0 – 0.3 – weak, rs = 0.3 – 0.7 – medium, rs > 0.7 – strong correlation. Qualitative data was analysed using a Pearson chi-square test or a Fisher's exact test according to their use. Binomial test was performed to test the proportions. A binary logistic regression analysis was used for the creation of prediction models and for the identifying of factors. The intraclass correlation coefficient (ICC) was used for the evaluation of the agreement of variables. A two-sided p-value of < 0.05 was considered to be statistically significant. Statistical analysis was performed using the IBM SPSS programme v.26 (*IBM, USA*) and R v.4.0.0 (*Vienna, Austria*).

2 Results

2.1 Description of the research sample

N = 53 patients participated in the research with their minimum age being 28 years and the maximum age being 85 years. The age range was 57 years with the average age M = 62.03; SD = 14.02 years, the median age of patients being 63 years, and the modal or most frequently occurring age being 77 years. A histogram of patient ages and a box-plot diagram are shown in Figure 2.1 a, b.

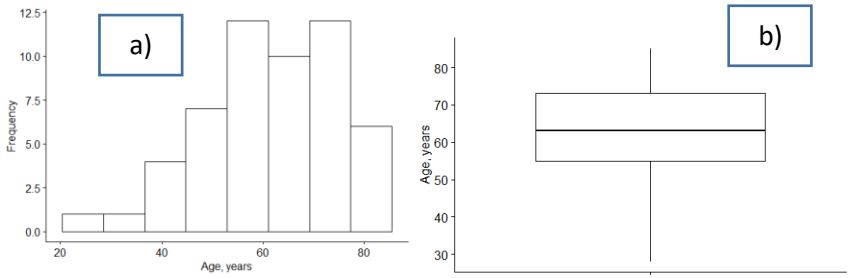


Figure 2.1 **Patient age a) histogram, b) box-plot diagram**

In analysing the age of the control group patients, it was found that the mean age was M = 64.80; SD = 8.92 years and was not different in statistical significance from the age of patients in the research (p = 0.32).

A description of the study group patients is shown in Table 2.1, and establishes that the number of males is statistically significantly larger than that of females (p < 0.001), and similarly the number of myopia, trauma and MS patients differs statistically significantly (p < 0.05), but the number of eye (OD or OS), glaucoma and PEX syndrome patients involved does not differ in a statistically significant way (p > 0.05).

In turn, the patients in the control group differ in a statistically significant way according to glaucoma, myopia, trauma and the PEX syndrome ($p < 0.001$).

Table 2.1

Patients characteristics: number and percentage (%)

Variable	Research group	Control group	Statistical significance
Gender			
Males Females	41 (77.4) 12 (22.6)	10 (32.3) 21 (67.7)	< 0.001***
Statistical significance	< 0.001***	0.07	
Eye			
OD OS	22 (41.5) 31 (58.5)	19 (61.3) 12 (38.7)	0.11 (n.s.)
Statistical significance	0.27 (n.s.)	0.28 (n.s.)	
Glaucoma			
Not present Present	30 (56.6) 23 (43.4)	29 (93.5) 2 (6.5)	< 0.001***
Statistical significance	0.41 (n.s.)	< 0.001***	
Myopia			
Not present Present	47 (88.7) 6 (11.3)	26 (83.9) 5 (16.1)	0.37 (n.s.)
Statistical significance	< 0.001***	< 0.001***	
Trauma			
Not present Present	36 (67.9) 17 (32.1)	29 (93.5) 2 (6.5)	0.007**
Statistical significance	0.01**	< 0.001***	
Marfan syndrome			
Not present Present	50 (94.3) 3 (5.7)	31 (100) 0 (0)	0.29 (n.s.)
Statistical significance	< 0.001***	–	
Pseudoexfoliation syndrome			
Not present Present	28 (52.8) 25 (47.2)	23 (74.2) 8 (25.8)	0.06 (n.s.)
Statistical significance	0.78 (n.s.)	0.01**	
Macular pathology			
Macular hole Epiretinal membrane	– –	17 (54.8) 14 (45.2)	–
Statistical significance		0.72 (n.s.)	

It can be established, from analysing the number of IOL manufacturers (Figure 2.2) that the *Tecnis ZCB00* was placed in the study group most frequently with 25 (47.11 %), while the *Alcon* and *Medicontur 877FABY* were placed in an equal number. In calculating the proportions for the number of manufacturers, it was established that all three IOL manufacturers used in the study were represented in equal numbers (p = 0.11), see Figure 2.2. Whereas, in the control group, the *Alcon* was the most frequently placed – 22 (70.97 %) and the *Medicontur*, the least, with only 2 cases (6.45 %).

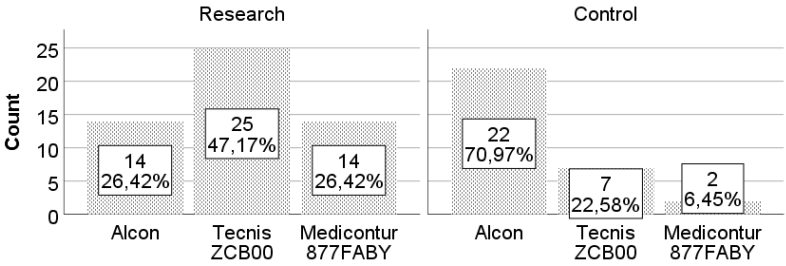
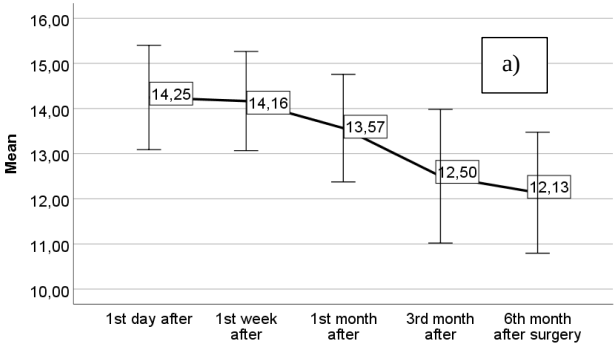


Figure 2.2 **The number of IOL manufacturers and the percentage**

2.2 Capsulorrhexis change analysis

The overall changes in the capsulorrhexis area after surgery are shown in Figure 2.3. It can be seen that the capsulorrhexis area reduces on average from 14.25 mm^2 to 12.13 mm^2 from the 1st day after surgery until the 6th month, which corresponds to 14.8 % percent of the initial value and these changes are statistically significant ($p < 0.001$). Whereas, the changes in the capsulorrhexis area 1 day after surgery and 1 month afterwards for the control group was on average from 18.29 mm^2 to 17.31 mm^2, which corresponds to 5.35 % ($p = 0.01$). Detailed changes in average values and standard deviations are portrayed in Table 2.2.



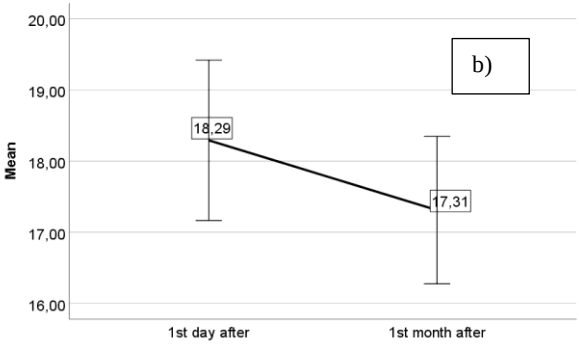


Figure 2.3 **Changes in the capsulorrhexis area (mm^2) in time after surgery for the a) research and b) control group**

Table 2.2

Dynamics of changes (mean and standard deviation) in the capsulorrhexis area (mm^2)

Time	Capsulorrhexis area	
	Research group	Control group
1 day after the op.	14.25 (2.86)	18.29 (3.07)
1 week after the op.	14.16 (2.72)	–
1 month after the op.	13.56 (2.94)	17.31 (2.82)
3 months after the op.	12.50 (3.66)	–
6 months after the op.	12.13 (3.32)	–
Statistical significance	< 0.001***	0.01**

Capsulorrhexis changes for the research group depending on the manufacturer are shown in Figure 2.4

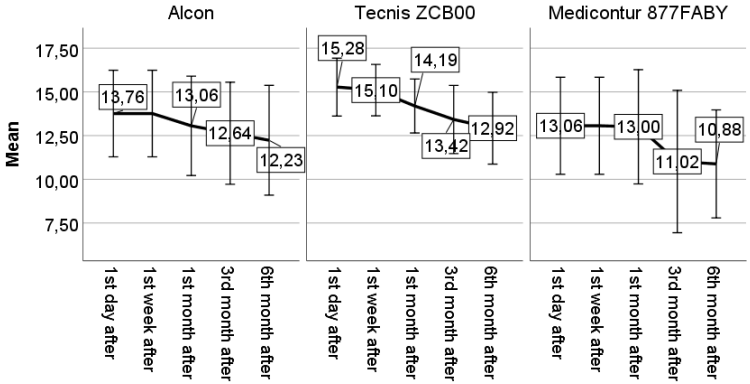


Figure 2.4 **Changes in the capsulorrhexis area (mm^2) for the study group after surgery depending on the IOL manufacturer**

In Table 2.3, it can be seen that the average capsulorrhexis area for the study group at different times post-surgery does not differ in a statistically significant way ($p > 0.05$), based on the IOL manufacturer. For example, 1 day after surgery, the average capsulorrhexis area for *Alcon* = 13.76 mm^2; for *Tecnis* = 15.12 mm^2; for *Medicontur* = 13.06 mm^2, and this difference is not statistically significant ($p > 0.05$). It is the same for the others in the post-surgery periods. A statistically significant difference ($p > 0.05$) in the capsulorrhexis area in a specific period, based on the manufacturer of the IOL, has not been established. However, a trend appears where an initially larger capsulorrhexis area appears with the *Tecnis ZCB00* and this reduces, but not to the average size of the area for both of the other manufacturers.

In analysing the capsulorrhexis area for the control group, it was established that a statistically significant difference was not found between IOL manufacturers 1 day after surgery ($p = 0.77$), and similarly, a difference was not found between IOL manufacturers 1-month post-surgery ($p = 0.97$).

Table 2.3

Mean values and standard deviations for capsulorrhexis changes, in time, for the control and research groups

Time	IOL Manufacturer	Research group	Control group
1 day after the op.	*Alcon*	13.76 (2.36)	18.10 (3.20)
	Tecnis ZCB00	15.12 (2.67)	18.48 (2.30)
	Medicontur 877FABY	14.12 (3.31)	19.71 (5.60)
	Statistical significance	0.27 n.s.	0.77 (n.s.)
1 week after the op.	*Alcon*	13.76 (2.36)	–
	Tecnis ZCB00	14.93 (2.34)	–
	Medicontur 877FABY	13.06 (3.31)	–
	Statistical significance	0.53 n.s.	–
1 month after the op.	*Alcon*	13.05 (2.70)	17.24 (3.10)
	Tecnis ZCB00	14.14 (2.54)	17.55 (2.36)
	Medicontur 877FABY	13.00 (3.90)	17.18 (1.85)
	Statistical significance	0.67 n.s.	0.97 (n.s.)
3 months after the op.	*Alcon*	12.63 (2.78)	–
	Tecnis ZCB00	13.04 (2.91)	–
	Medicontur 877FABY	11.01 (4.87)	–
	Statistical significance	0.78 n.s.	–
6 months after the op.	*Alcon*	12.23 (2.90)	–
	Tecnis ZCB00	12.56 (3.31)	–
	Medicontur 877FABY	10.88 (3.70)	–
	Statistical significance	0.15 n.s.	–

In analysing the capsulorrhexis area's percentage increase in time, compared with 1 day after surgery (see Table 2.4), it was established that the capsulorrhexis area reduced the slowest for the *Alcon* manufacturer – after 6 months, the capsulorrhexis area reduced on average by 11 % of the initial value, but for the *Tecnis* and *Medicontur* manufacturers the reduction of the capsulorrhexis area was about the same and it reduced by about 16 % of the initial value 6 months after surgery.

Table 2.4

The percentage (%) reduction in the capsulorrhexis area, in time, for the study group, 1 day after surgery, depending on the manufacturer

IOL manufacturer	1 day after the op.	1 week after the op.	1 month after the op.	3 months after the op.	6 months after the op.
Alcon	–	0	5.08	8.10	11
Tecnis ZCB00	–	1.25	6.41	13.75	16.86
Medicontur 877FABY	–	0	5.23	15.62	16.70

Whereas in analysing the percentage changes in capsulorrhexis for the control group, depending on the manufacturer, it was established that the greatest changes were for *Medicontur 877FABY*, which constituted 12.83 % (see Table 2.5).

Table 2.5

Percentage (%) reduction in the capsulorrhexis area for the control group, in time, depending on the IOL manufacturer with respect to 1 day post-surgery

IOL manufacturer	1 day after the op.	1 month after the op.
Alcon	–	4.75
Tecnis ZCB00	–	5.30
Medicontur 877FABY	–	12.83

Changes in the capsulorrhexis area, in time, are shown in Figure 2.5, where the patients in the research group had a trauma (the average reduction between 15.57 mm^2 and 12.72 mm^2, which corresponds to a reduction of 18.30 %), and if the patient did not have a trauma (from 13.66 mm^2 to 11.87 mm^2,

and the reduction, correspondingly – 13.10 %). It can also be noted that in the case of a trauma, the initial capsulorrhexis field post-surgery is, on average, larger by 1.91 mm^2 than for patients who have not had a trauma.

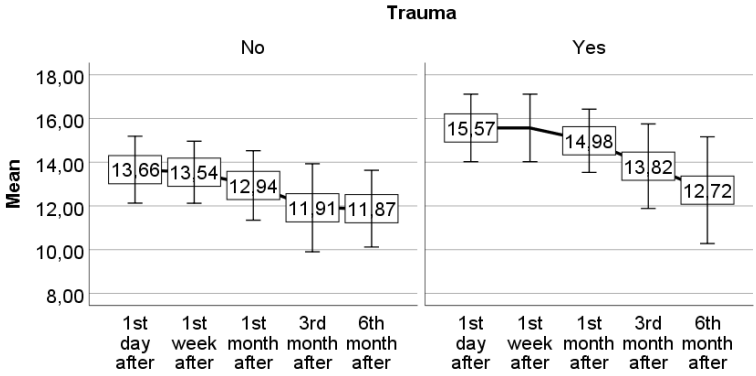


Figure 2.5 **Changes in the capsulorrhexis area (mm^2) for the research group post-surgery, in time, depending on trauma**

As can be seen in Figure 2.6, if the diameter of the CTR is 11 mm, then the capsulorrhexis area reduces from the initial average of 13.70 mm^2 to 10.58 mm^2 after 6 months, and this corresponds to a reduction of 22.7 %; whereas, if the diameter of the CTR is 12 mm, then the capsulorrhexis area reduces to 13.43 mm^2, from the initial average of 14.61 mm^2, which corresponds to 8.07 %.

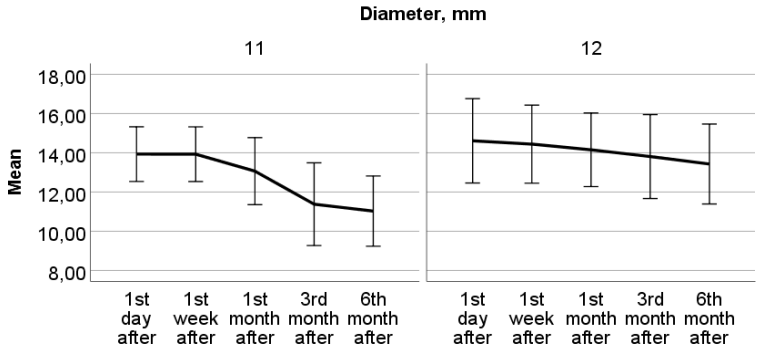


Figure 2.6 **Changes in the capsulorrhexis area (mm^2) for the research group, in time, depending on the diameter**

As can be seen in Figure 2.7, if the capsular ring type is a CTR, then the capsulorrhexis field reduces to 11.30 mm^2 from an initial average value of 13.90 mm^2, which corresponds to a reduction of 18.70 %, but with a mCTR (Cionni), the initial average capsulorrhexis area reduces from 14.65 mm^2 to 13.33 mm^2, corresponding to 9.01 %.

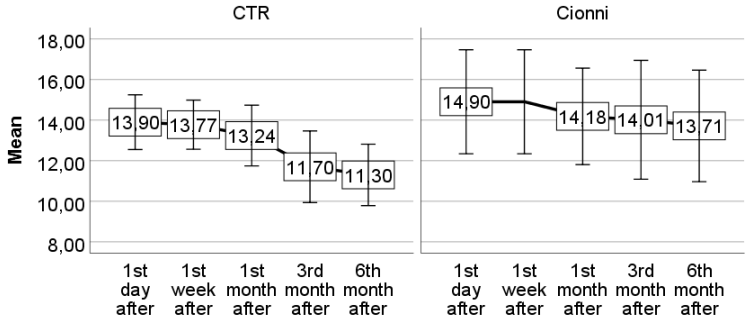


Figure 2.7 **Changes in the capsulorrhexis area (mm^2) for the research group, in time, depending on the type of capsular ring**

As can be seen in Figure 2.8, if the patients have pseudoexfoliation syndrome, then the capsulorrhexis field reduces to 12.16 mm^2 from an initial average value of 14.56 mm^2, which corresponds to a reduction of 16.48 %.

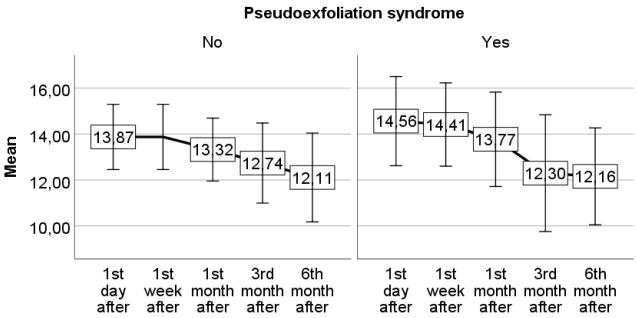


Figure 2.8 **Changes in the capsulorrhexis area (mm^2) for the research group, in time, depending on pseudoexfoliation syndrome**

2.3 Analysis of the difference in the capsulorrhexis area for the research group in comparison to the control group, 1 month post-surgery

Calculations show that the median difference in the capsulorrhexis area for the research group 1 month post-surgery is −0.42 [−0.03 – −2.16] mm^2, whereas, the median for the control group it is −0.49 [0.00 – −1.70] mm^2. A statistically significant difference has not been established ($p > 0.05$). However, an overall trend can be observed that the capsulorrhexis field for the majority of the research group patients, 1 month post-surgery, is larger than for control group patients (see Figure 2.9).

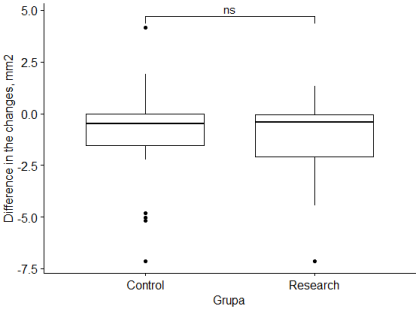


Figure 2.9 **Difference in the changes in the capsulorrhexis area (mm^2) after 1 month for the control and the research groups**

In analysing the difference in the capsulorrhexis area based on secondary illnesses, it can be established that there are statistically significant changes 1 month post-surgery for control group patients with myopia and pseudoexfoliation syndrome ($p < 0.05$), see Table 2.6.

Table 2.6

Analysis of the differences (median and interquartile range) in changes in the capsulorrhexis area, 1 month post-surgery

Comorbidity	**Difference in the changes in the capsulorrhexis after 1 month, mm^2**	
Group	**Research**	**Control**
Glaucoma		
Not present	−0.44 [−0.02 – −2.00]	−0.49 [−0.02 – −1.71]
Present	−0.42 [−0.04 – −2.48]	−0.36 [−0.1 – −0.77]
Statistical significance	0.92 (n.s.)	0.68 (n.s.)
Myopia		
Not present	−1.70 [0.33 – −6.10]	−0.41 [0.00 – −1.25]
Present	−0.06 [−0.02 – −2.06]	0.33 [0.33 – −6.10]
Statistical significance	0.70 (n.s.)	0.03
Trauma		
Not present	−0.35 [−0.03 – −2.23]	−0.55 [–0.02 – −1.71]
Present	−0.47 [–0.07 – –1.61]	−0.22 [−0.10 – −0.49]
Statistical significance	0.48 (n.s.)	0.61 (n.s.)
Marfan syndrome		
Not present	−0.42 [−0.03 – −2.22]	−0.49 [0.00 – −1.70]
Present	−0.45 [−0.01 – −0.87]	–
Statistical significance	0.57 (n.s.)	–
Pseudoexfoliation syndrome		
Not present	−0.55 [−0.04 – −1.62]	−0.28 [0.05 – −0.67]
Present	−0.26 [−0.01 – −2.28]	−1.57 [–0.80 – −4.33]
Statistical significance	0.53 (n.s.)	0.03

After analysing differences in changes to the capsulorrhexis area 1 month post-surgery, and dividing the control and the research groups by manufacturer, it was established that the changes were not different in a statistically significant way ($p > 0.05$), see Figure 2.10.

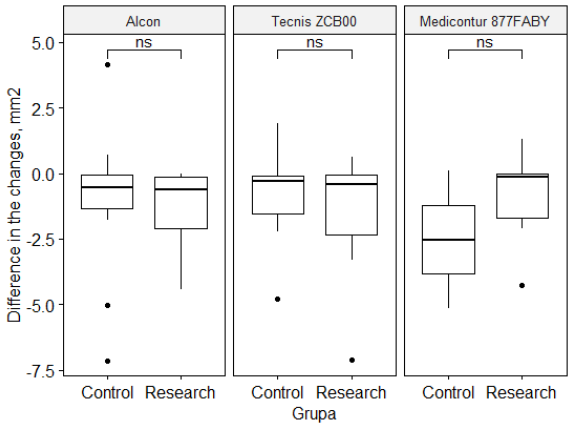


Figure 2.10 **Analysis of the differences in changes in the capsulorrhexis area, 1 month post-surgery, based on the IOL manufacturer**

After analysing the correlation between the age of patients in the control and study groups and the differences in the capsulorrhexis area, 1 month post-surgery, a statistically significant correlation could not be established ($p > 0.05$), see Figure 2.11.

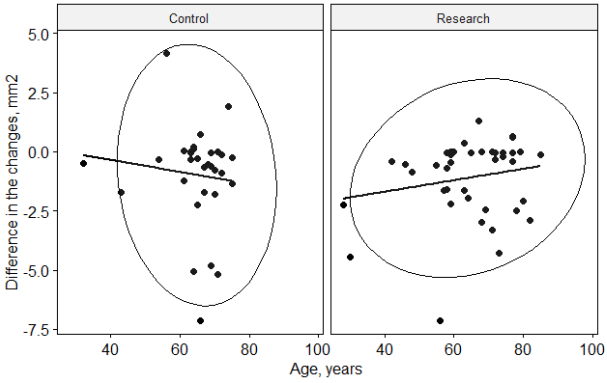


Figure 2.11 **Correlation diagram on the age of control and research group patients and differences in the capsulorrhexis area, 1 month post-surgery**

2.4 Analysis of differences in the capsulorrhexis area for research group patients, 3 months post-surgery

The capsulorrhexis area for the study group patients with glaucoma, reduced after 3 months in a more statistically significant ($p = 0.01$) way than for those who did not have glaucoma. Statistically significant differences were not established in the capsulorrhexis area after 3 months for myopia, trauma or Pseudoexfoliation syndrome patients ($p > 0.05$), see Table 2.7.

Table 2.7

Analysis of differences in changes to the capsulorrhexis area (median and interquartile range) for the research group after 3 months

Comorbidity	**Differences in changes to the capsulorrhexis after 3 months, mm^2**	**Statistical significance**
Glaucoma		
Not present Present	−1.30 [–0.07 – −2.33] −2.50 [−1.72 – −4.86]	0.01**
Myopia		
Not present Present	−2.00 [–0.88 – −2.98] −1.14 [−0.03 – −4.37]	0.75 (n.s.)
Trauma		
Not present Present	−2.23 [−0.15 – −4.74] −1.79 [−1.45 – −2.31]	0.44 (n.s.)
Marfan syndrome		
Not present Present	−1.86 [−0.27 – −3.56] −2.20 [−0.10 – −2.48]	0,78 (n.s.)
Pseudoexfoliation syndrome		
Not present Present	−1.76 [−0.52 – −2.50] −2.46 [−0.40 – −2.86]	0.19 (n.s.)

Box-plot diagrams of differences in the capsulorrhexis area after 3 months are shown in Figure 2.12.

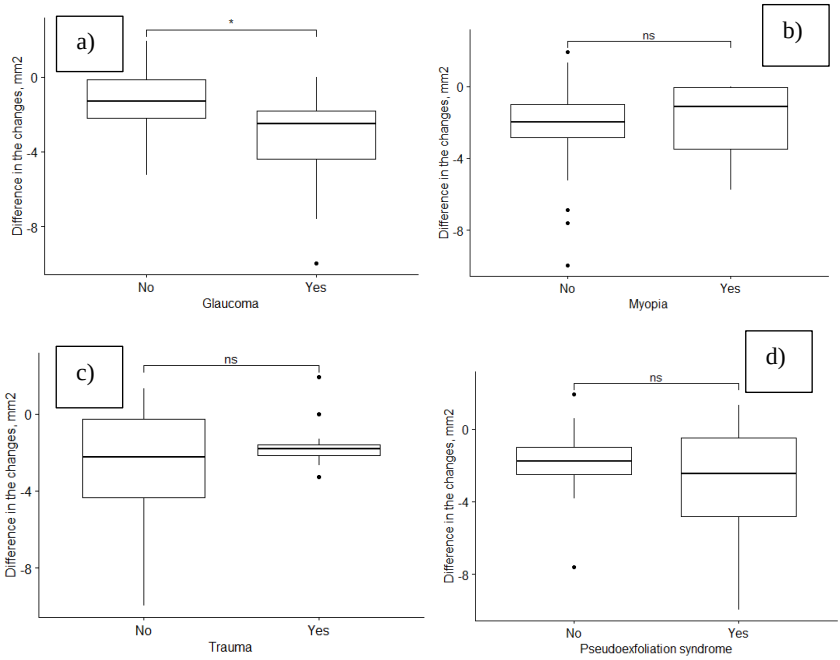


Figure 2.12 **Differences in the capsulorrhexis area, 3 months post-surgery for a) glaucoma, b) myopia, c) trauma, and d) Pseudoexfoliation syndrome**

As can be seen in Figure 2.13, if the patients do not have PEX syndrome, then a statistically significant correlation is not found ($p = 0.52$) between the length of the surgery and changes to the capsulorrhexis area after 3 months, but a statistically significant correlation ($rs = 0.32$; 95 % TI: 0.09 – 0.63; $p < 0.05$) between these variables can be observed for patients with PEX syndrome. The longer the operation, the smaller the changes will be to the capsulorrhexis area, 3 months post-surgery, respectively.

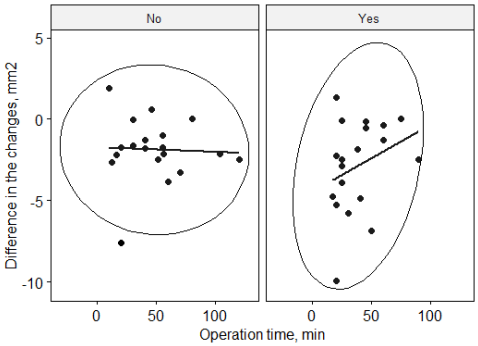


Figure 2.13 **Correlation diagram for differences in the capsulorrhexis area after 3 months post-surgery and the length of the operation for Pseudoexfoliation syndrome – No/Yes**

2.5 Model for the prediction of differences in the capsulorrhexis area for research group patients, 3 months post-surgery

An input analysis of various factors was undertaken regarding differences in the size of changes to the capsulorrhexis area, 3 months post-surgery, using the assistance of linear regression, which established that the following predictors could be included in the model: the eye of the patient involved, the diameter of the CTR, glaucoma and trauma. All of the predictors included in the model have a statistically significant effect on the changes to the capsulorrhexis area ($p < 0.05$) after 3 months. Of these factors, the eye and the diameter of the CTR (corresponding standardised coefficient = 0.56 and 0.53) have the greatest involvement in predictions of changes to the capsulorrhexis area after 3 months, while trauma has the least (standardised coefficient = 0.24). The model obtained is statistically significant ($p < 0.001$) and the coefficient of determination which was obtained was $R^2 = 57$ % (95 % TI: 39 – 77 %). The predictor effect model is shown in Table 2.8, with this equation: Difference of the capsulorrhexis area for the research group, 3 months post-surgery = –4.64 + 2.87 × Eye involved + 2.47 × Diameter – 2.03 × Glaucoma + 1.10 × Trauma.

Table 2.8

Model for the prediction of the difference of the capsulorrhexis area for the research group, 3 months post-surgery

Variable	Coefficient B (95 % TI)	Statistical significance	Standardised coefficient B
Intercept	−4.64 (−3.29 – −5.98)	< 0.001***	
Eye involved	2.87 (1.68 – 4.06)	< 0.001***	1.19
Diameter	2.47 (1.30 – 3.65)	< 0.001***	1.02
Glaucoma	−2.03 (−0.92 – −3.15)	< 0.001***	−0.84
Trauma	1.10 (0.03 – 2.27)	0.04*	1.10

An intraclass correlation coefficient was calculated to evaluate the calculated model's agreement with the difference in the real capsulorrhexis area, 3 months post-surgery, revealing that the reliability between the real value and the calculated statistical evaluation was good (ICC = 0.72; 95 % TI: 0.53 – 0.84).

A second regression model was created within the framework of the Doctoral Thesis, which predicted the real value of the capsulorrhexis area 3 months post-surgery. As a result, it was found that the following predictors could be included in the model: the capsulorrhexis area 1 day post-surgery, the eye involved, the diameter of the CTR and glaucoma. All of the predictors included in the model have a statistically significant effect on the capsulorrhexis area's 3 months post-surgery value ($p < 0.05$). Of these factors, the greatest change in the capsulorrhexis area after 3 months was predicted by – the capsulorrhexis area 1 day post-surgery (standardised coefficient = 0.89) and the eye involved (standardised coefficient = 0.65). The model obtained is statistically significant ($p < 0.001$) and the obtained coefficient of determination $R^2 = 87$ % (95 % TI: 77 – 94 %). The predictor effect model is shown in Table 2.9., with this equation: Capsulorrhexis area for the research group, 3 months post-surgery = –5.35 + 1.08 × Capsulorrhexis area 1 day after op. + 2.97 × Involved eye + 2.32 × Diameter – 2.20 × Glaucoma.

Table 2.9

Model for the prediction of the capsulorrhexis area for the research group, 3 months post-surgery

Variable	Coefficient B (95 % TI)	Statistical significance	Standardised coefficient B
Intercept	–5.35 (−8.07 – −2.63)	< 0.001***	–
Capsulorrhexis area 1 day after op.	1.08 (0.07 – 0.24)	< 0.01**	0.89
Involved eye	2.97 (1.71 – 4.23)	< 0.001***	0.65
Diameter	2.32 (1.11 – 3.54)	< 0.001****	0.51
Glaucoma	−2.20 (−3.34 – −1.05)	< 0.001***	−0.48

An intraclass correlation coefficient was calculated to evaluate the agreement of the calculated model's value with the real capsulorrhexis area, 3 months post-surgery, and indicated that the agreement between the real value and the calculated one was excellent (ICC = 0.93; 95 % TI: 0.87 – 0.96). In the same way too, a *Bland-Altman* plot was created (Figure 2.14) to evaluate the accuracy of the created regression model, which showed the difference between each patient's real and calculated value, and as can be observed, bias was not observed in the regular calculated value result in relation to the real capsulorrhexis area, 3 months post-surgery. The average values for both test results were also not different in a statistically significant way ($p > 0.05$).

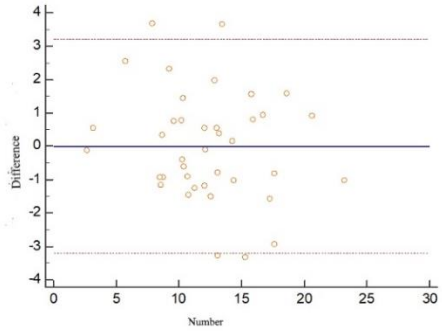


Figure 2.14 ***Bland-Altman* plot**

2.6 Surgery time analysis

After analysing the time of surgery for the research group, it was found that the minimal length of surgery was 10 minutes and the maximum – 120 minutes, with the average time of surgery being – 42.33; SD = 24.32 minutes, the median – 40 minutes, the modal or most frequently encountered time of surgery – 20 minutes, the first quartile – 20 minutes, the third – 55 minutes, with the time of surgery interquartile range being – 35 minutes (see Figure 2.15 a).

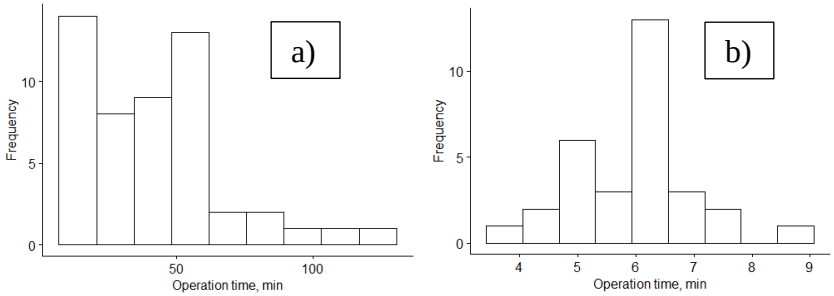


Figure 2.15 **Time of surgery histogram for patients in the a) research group and the b) control group**

After analysing the time of surgery for the control group, it was established that the minimum time of surgery was 4 minutes, the maximum – 9 minutes, the average length of surgery – 6.00; SD = 1.05 minutes, the median – 6 minutes, the modal or most frequently encountered time of surgery – 6.50 minutes, the first quartile – 5 minutes, the third – 6.50 minutes, with the time of surgery interquartile range being – 1.50 minutes (see Figure 2.15 b).

In analysing the time of surgery for the control group with the various manufacturers, it was established that the median time of surgery with *Alcon* was 50.00 minutes [22.50 – 54.00], with *Tecnis* 45.00 minutes [25.00 – 59.00] and with *Medicontur* 25.00 minutes [20.00 – 44.50]. The statistical analysis did

not find that the time of surgery was dependent on the manufacturer of the lens in a statistically significant way (p = 0.50), see Figure 2.16.

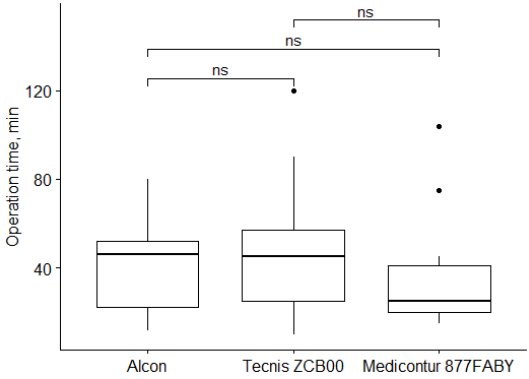


Figure 2.16 **Time of surgery for the research group in a box plot diagram for various IOL manufacturers**

After analysing the time of surgery for patients in the research group using a Mann-Whitney test, a statistically significant difference for either gender, the eye, or trauma was not found (p > 0.05), see Table 2.10. However, the median time of surgery in a case of trauma is slightly greater than in a case where there is no trauma (45 as opposed to 35 minutes respectively), even though a statistically significant difference was not found (p = 0.20). Whereas, with the presence of pseudoexfoliation syndrome, the median time of surgery was half as long (50 as opposed to 25 minutes, respectively) and a statistically significant difference was found (p = 0.03). Similarly, the mCTR had a statistically significant (p < 0.001) longer time of surgery, an operation which was about twice as long than with a CTR.

Whereas, a statistically significant difference between the various parameters was not found for the control group (p > 0.05), see Table 2.10.

Table 2.10

Time of surgery (median and interquartile range) analysis

Variable	Time of surgery in minutes	
	Research group	**Control group**
Gender		
Males	45.00 [21.25 – 52.50]	6.25 [5.00 – 7.00]
Females	30.00 [20.00 – 79.00]	6.00 [5.00 – 6.50]
Statistical significance	0.93 (n.s.)	0.84 (n.s.)
Eye		
OD	47.50 [20.00 – 62.50]	6.00 [5.00 – 7.00]
OS	38.00 [25.00 – 50.00]	6.00 [5.00 – 6.50]
Statistical significance	0.31 (n.s.)	0.99 (n.s.)
Trauma		
Not present	35.00 [20.00 – 50.25]	6.00 [5.00 – 6.50]
Present	45.00 [27.50 – 72.50]	5.75 [5.00 – 8.50]
Statistical significance	0.20 (n.s.)	0.86 [n.s.]
PEX syndrome		
Not present	50.00 [30.00 – 57.00]	6.00 [5.00 – 6.50]
Present	25.00 [20.00 – 47.50]	6.00 [5.62 – 6.50]
Statistical significance	0.03*	0.99 (n.s.)
Type of capsular ring		
CTR	22.50 [17.75 – 30.00]	–
mCTR(Cionni)	54.00 [50.00 – 63.75]	
Statistical significance	< 0.001***	–
Glaucoma		
Not present	48.00 [20.00 – 59.00]	6.00 [5.00 – 6.50]
Present	30.00 [20.00 – 50.00]	7.00 [6.50 – 7.00]
	0.16 (n.s.)	0.84 (n.s.)

After analysing the time of surgery with the CTR and mCTR (Cionni) types of capsular rings, it was found that the mCTR (Cionni) had a statistically significant longer time of surgery than the CTR ($p < 0.001$), see Figure 2.17.

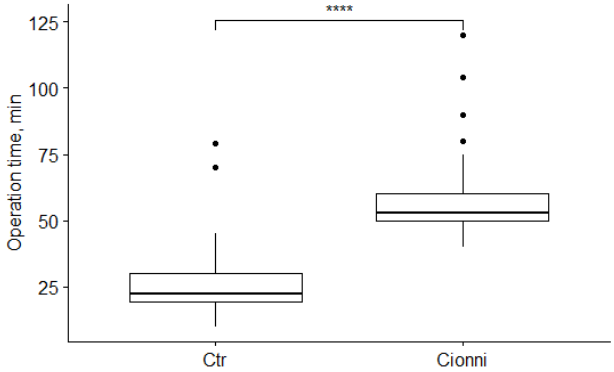


Figure 2.17 **Time of surgery for the research group patients in a box-plot diagram for CTR and mCTR (Cionni)**

Connections between the age of research group patients and the time of surgery are shown separately in Figure 2.18 a, b, c, d for 1) presence or absence of glaucoma, 2) PEX syndrome, 3) OD and OS eyes, and 4) presence or absence of trauma. Statistical analysis found that a trend towards a negative correlation had been maintained in all variables (the greater the age of the patient, the shorter the length of surgery), but a statistically significant difference in correlation strength between the groups (presence or absence of glaucoma and presence or absence of PEX syndrome, etc.) ($p > 0.05$) was not found.

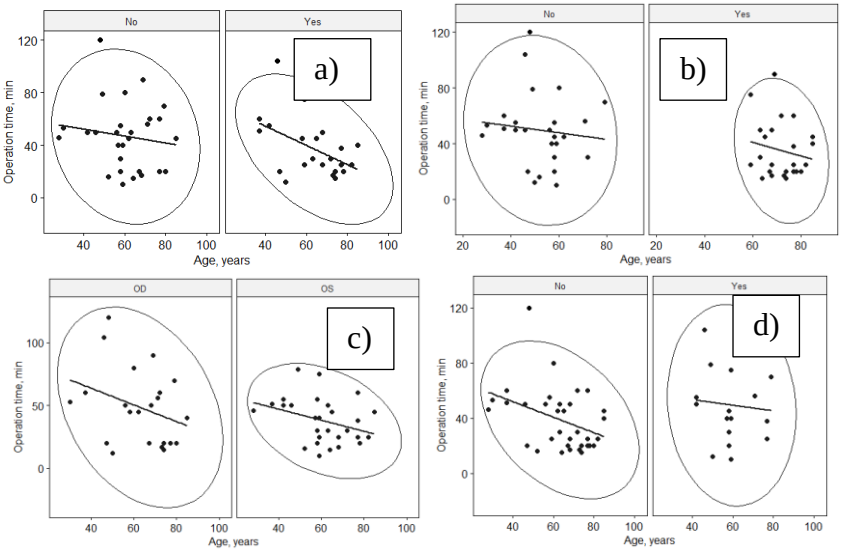


Figure 2.18 **Correlation diagram between the age and time of surgery for research group patients a) with presence or absence of glaucoma, b) with presence or absence of PEX syndrome, c) OD and OS eyes d) with presence or absence of trauma**

2.7 Characterisation of late IOL-CTR-capsular bag dislocation patients

In the period from 2011 (commencement of the research) to March 2020, late IOL-CTR-capsular bag dislocation was observed for 7 patients (13.2 %). The average late IOL-CTR-capsular bag dislocation period was 57.42 months (SD 35.64 months), the minimum – 12 months, the maximum – 96 months and the median – 60 months [Q1 – Q3: 24 – 96 months].

For late IOL-CTR-capsular bag dislocation patients, the reduction in the anterior capsular opening was 32.7 % (13.09 mm^2 to 8.80 mm^2) in the 6-month observation period, see Figure 2.19.

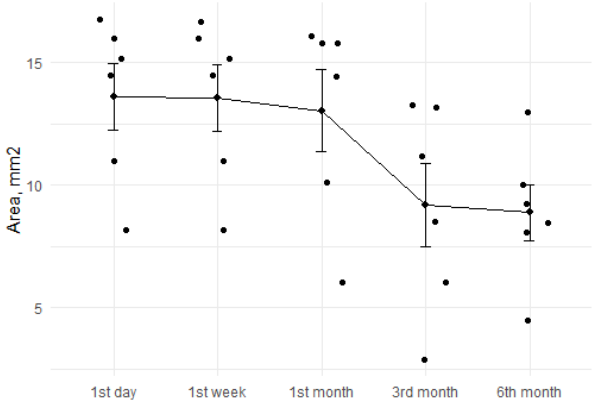


Figure 2.19 **Reduction in the anterior capsular opening for late IOL-CTR-capsular bag dislocation patients**

An anterior capsular Nd:YAG lasercapsulotomy was undertaken for 8 of the 53 (15.1 %) patients due to marked phymosis. Four of these 8 patients had PEX syndrome, 5 glaucoma, 1 trauma and 1 Marfan syndrome, 1 myopia, with combinations of these factors as well.

The median time point of the Nd:YAG anterior capsulotomy was 4.5 months, the minimum – 1 month, the maximum – 48 months (Figure 2.20), with 2 of the 8 patients having a late IOL-CTR-capsular bag dislocation.

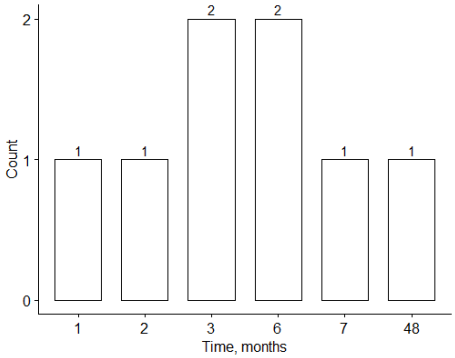


Figure 2.20 **Time point of Nd:YAG anterior lasercapsulotomy for anterior capsular opening phymosis patients**

Reduction in the anterior capsular opening for Nd:YAG anterior capsulotomy patients was 32.6 % (13.46 mm^2 to 9.06 mm^2) (Figure 2.21) in the 6-month observation period.

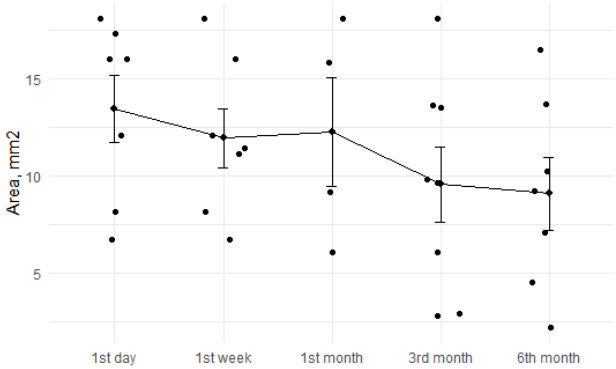


Figure 2.21 **Reduction in the anterior capsular opening for Nd:YAG anterior capsulotomy patients**

3 Discussion

The number of patients (53) included in the research, who were operated on, do not reflect the total number of patients who have a subluxated lens or zonular weakness, as intraoperatively diagnosed patients with zonular weakness were not included in the research, and there was also no data about surgery performed on patients with similar diagnoses at other clinics. In Denmark, a prevalence 6.4/100,000 patients with congenital ectopia lentis was reported, for 31 % of whom the nosological origin could not be determined, but for 69 % patients it was associated with Marfan syndrome (MS) (68.2 %), ectopia lentis et pupillae – 21.2 %, autosomal dominant ectopia lentis – 8 %, homocystinuria – 1.1 %, sulphite-oxidase deficiency – 0.7 %, or Weil-Marchesani syndrome – 0.7 % (Fuchs & Rosenberg, 1998). In total, 396 patients for whom diagnosis was determined in the period from 1977 to January 1993 were included in the study. Subluxated lenses with a traumatic origin were indicated in 100 patients within the same time frame (Fuchs & Rosenberg, 1998). Khokhar et al. reported 71 traumatic lens subluxations from 150 cases of subluxated lenses, which were operated on at a tertiary ophthalmological clinic in northern India in the period from October 2009 to September 2011, although there was no data about the total number of cataract operations in the same time period to speculate about the prevalence of subluxation (Khokhar et al., 2014). Shah et al. reported about 59 cases of traumatic subluxated lenses in Larkana, Pakistan – over a 13-year period, even though the total numbers of patients who were consulted and operated on, were not indicated (Shah et al., 2016).

Whereas, zonular weakness associated with PEX syndrome, which is also included in this research as lens subluxation, was registered in 159 of 3,000 patients with PEX syndrome who were operated on in the period from 1988 to 2010 in research at one centre in Massachusetts, USA (Shingleton et

al., 2017). In north western Spain, in a research period from 2009 to 2010, zonular weakness was found in 7 PEX syndrome patients of the 120 patients with this diagnosis. Overall, 503 patients (Vazquez-Ferreiro et al., 2019) were operated on at this centre and these results were similar to research undertaken in Portugal, where phacodonesis was found in 5 of the 43 PEX syndrome patients in a group of 183 cataract patients in a 6-month period (Alfaiate et al., 1996). From the 9,528 patients operated on in Munich Germany in a five year period, 69 or 0.7 % required implantation of a CTR due to zonular insufficiency, of whom 40 or 58 % also had zonular insufficiency of unknown origin (including patients with completely mature (*matura*) cataracts, those after a vitrectomy with silicon oil, and serious myopia), 23 or 33 % with a post traumatic cataract, 4 eyes or 6 % – with PEX syndrome, and 2 eyes or 3 % – Marfan syndrome (Tribus et al., 2007).

Whereas, in Japan in the period from 1999 to 2007, 75 patients (80 eyes) were identified with an implanted CTR, indicating zonular weakness, even though the total number of cataract operations at the clinic where the research was done were not shown. The reasons for the zonular weakness were as follows – PEX syndrome (31 %), anterior chamber angle closure or angle closure glaucoma (25 %), trauma (17 %), surgical complications (6.4 %), chronic uveitis (4.3 %), post-vitrectomy (4.3 %), congenital anomalies (4.3 %) and unknown reasons (6.4 %) (Takimoto et al., 2008). In a study performed in Turkey, of the 4,316 cataract operations conducted in a 3-year period (2010 – 2013), 41 eyes or 0.94 % of patients required a CTR implantation due to zonular weakness (Celik et al., 2015) where the main reasons were mature cataracts (29.2 %), traumatic cataracts (24.3 %), PEX syndrome (19.5 %), retinitis pigmentosa (14.6 %), degenerative myopia (9.7 %), and lens coloboma in (2.4 %).

Lens subluxation of traumatic origin was found in 17 or 32.1 % of research patients from the anamnesis data, but without documented

confirmation of closed or open eye trauma. Lens subluxation was established relatively rarely in cases of blunt eye trauma (Canavan & Archer, 1982; Macewen, 1989), and was usually in combination with injury to parts of the eye; for example, iridodialysis, recession of the angle of the anterior chamber, ciliary body dialysis, choroidal rupture, retinal dialysis or retinal tear and detachment, hyphaema or haemophthalmus (Canavan & Archer, 1982; Viestenz & Kuchle, 2004). Khokhar et al. established lens subluxation as a result of trauma in approximately half of the patients studied (71 of 150), where lens subluxation was as a result of blunt trauma in 89 % , with 11 % as a result of penetrating trauma (Khokhar et al., 2014). In Larkana, Pakistan, 59 patients with traumatic lens subluxation (6 with a penetrating injury) were treated in a 13-year period from 2002 to 2015, but the total number of patients treated in this period, who had lens subluxation, was not indicated (Shah et al., 2016). The study in Denmark revealed 18 % traumatic lens subluxation (100 patients of the 568 included in the research) (Fuchs & Rosenberg, 1998), which is similar to the results of the current study. Trauma was mentioned, in phase III surgical survey sponsored by *Opthec USA*, as a reason for lens subluxation for 47 of 224 subluxated lens patients, who had a CTR implanted (Price et al., 2005).

PEX syndrome was established in 47.2 % or 25 of the total patient number. The prevalence of PEX syndrome differs in various regions around the world – in Estonia, it is reported in 25.5 % of the population with an average age of 70 years (Kaljurand & Teesalu, 2010). The prevalence of PEX syndrome in planned cataract operation patients in Estonia was even greater – 35.4 %. The syndrome was observed in 17.6 % of the 50–59 year-olds age group and 38.6 % in the 80–89 year-olds age group (Kaljurand & Puska, 2004). Cases of zonular weakness or subluxation were not reported. In Finland, the prevalence of PEX syndrome was 31 %, and it was found that PEX syndrome patients have a 10 times greater risk of lens capsular loss during cataract surgery, indicating

zonular weakness, even though lens subluxation due to PEX syndrome was not separately categorised (Lumme & Laatikainen, 1993). In northern Sweden, PEX syndrome was established in at least 1 eye for 66 year-old patients in 23 % cases, and was more pronounced for females (29 %) than for males (15 %) (Astrom & Linden, 2007). In Portugal, PEX syndrome was reported in 23.5 % of patients with an average age of 75.98 years in a study group with 183 patients, with 16.1 % of PEX syndrome patients having phacodonesis established during cataract surgery, indicating lens subluxation and zonular weakness, while phacodonesis was not established in the control group (Alfaiate et al., 1996). In north western Spain, PEX syndrome was established in 17.4 % of cataract surgery patients, with a total of 730 cataract operations being conducted in the study period from 2009 to 2010 (Vazquez-Ferreiro et al., 2019). Phacodonesis or conclusive lens subluxation was not separately categorised, but zonular dialysis, which is a sign of zonular weakness, was established intra-operatively in 7 cases of 120 eyes with PEX syndrome (Vazquez-Ferreiro et al., 2019). In the state of West Bengal in India, PEX syndrome was established in 512 or 15.53 % of the 3,334 cataract surgeries that were conducted in a 3.5-year period from 2013 to 2016. A characteristic tendency for the increased prevalence of PEX syndrome with an increase in the age of patients was also observed (Islam et al., 2017). Lens subluxation was not established for any patients during pre-surgery examination, even though 7 patients had zonular dialysis during cataract surgery, while 23 patients or 4.49 % had a dislocation of the IOL over a 3-month period, which the authors link with existing zonular weakness (Islam et al., 2017).

In another study conducted in India analysing 1.5 years of cataract surgery data for 2016–2017 PEX syndrome was established in 22.1 % (226 patients) of 1,022 patients; 5.3 % of these (12 patients) were defined as patients with lens subluxation. During surgery, 6 patients also had intra-operatively diagnosed zonular weakness, and as a consequence, 18 or 8 % in total of all

PEX syndrome patients had a CTR implanted (Joshi & Singanwad, 2019). 159 of 3,000 PEX syndrome patients, who had cataract surgery, had zonular weakness established preoperative or intraoperative in Massachusetts, USA over a 22-year period, even though the total number of operated patients, or the prevalence of PEX syndrome, was not indicated (Shingleton et al., 2017). PEX syndrome was the main cause of lens subluxation in phase III clinical study on CTRs, and constituted 44 % of the study group (113 of 224 patients) (Price et al., 2005), which is similar to that in the present study.

Study by *Hayashi et al.*, where the influence of hydrogel and acrylic lenses on anterior capsular contraction were compared, clearly established that anterior capsular contraction over a 3 to 6-month period for hydrogel lenses was more pronounced than for acrylic lenses. Six months after surgery, the average contraction of hydrogel lenses was 16.9 %, as opposed to 8.8 % for acrylic lenses (Hayashi et al., 2001). In another study which compared the anterior capsular percentage reduction between silicone and acrylic lenses, it was 21.6 % for silicone lenses and 15.8 % for acrylic lenses over a 6-month period (Hayashi & Hayashi, 2005). The impact of hydrophilic or hydrophobic acrylic material on the anterior capsule did not differ overall, even though hydrophobic acrylic lenses have a greater surface adhesion than hydrophilic acrylic lenses with the lens capsule (Kugelberg et al., 2008; Ursell et al., 2018), which was confirmed by a 3-year survey by Becker et al., with hydrophilic acrylic lenses, which did not establish significant changes to the anterior capsular opening area, maintaining a stable 25 % IOL anterior area covering (Becker et al., 2006).

However, Žemaitiene et al. reported a different result, with hydrophilic acrylic lenses creating greater anterior capsular fibrosis than hydrophobic over a 1-year period (Zemaitiene et al., 2008), as did the research by Tsinopoulos et al., where hydrophobic acrylic lenses were compared with hydrophilic, revealing significant anterior capsular fibrosis with contraction for 4 patients

(of 273) in the hydrophobic acrylic lens group, as opposed to 19 (of 366) in the hydrophilic acrylic lens group (Tsinopoulos et al., 2010).

The polishing of LEC from the lens' anterior capsule over a 3-year period created less anterior capsule opacification and fibrosis in the eyes without secondary illnesses in a standard sized (5 mm diameter) capsulorrhexis, creating 15 % and 19 % subjectively defined anterior capsule opacification in 2 different intra-ocular lens groups (hydrophobic silicone with a rounded edge to the optical part, with the angle of the haptic part being different in relation to the optical part) in which polishing of the anterior capsule was undertaken, against 26 % and 26 % in the same lens groups, where polishing of the anterior capsule was not undertaken (Sacu et al., 2004), and this tendency to opacification of the anterior capsule was also confirmed in the 5-year observation of a lens of similar design (hydrophobic silicone with an angled haptic part, but sharp edged optics), where the only statistically significant changes were the subjectively determined degree of opacification of the anterior capsule (Bolz et al., 2006). In both studies, none of the study patients had a damaged anterior capsule or zonules, and no cases of a marked reduction to an anterior capsular opening were established; even though, considering the opacification of the anterior capsule between the polished and the unpolished anterior capsule groups, it was concluded that the polishing of the anterior capsule would avert prospective marked capsular fibrosis (Bolz et al., 2006; Sacu et al., 2004).

In a study by Shah et al., with 60 patients and 120 healthy eyes without other secondary illnesses (except cataracts), in which a hydrophobic acrylic lens was implanted, statistically significant increased opacification of the anterior capsule was established 1 month post-surgery in the group where polishing of the anterior capsule's LEC was not undertaken; even though the incidence of opacification of the anterior capsule had evened out between the groups in the 6-month period, where the polishing of the LEC was and was not

undertaken (Shah et al., 2009). Grade IV anterior capsule opacification or marked capsule contraction was observed in 2 patients (3.3 %) from the group in which polishing of the anterior capsule's LEC was not undertaken 1 month post-surgery, and additional cases were no longer observed in other visits in any of the groups. In the same study, the authors reported statistically significant increased marked post-operative indicators of inflammation (*cells and flare*) in the group where polishing of the anterior capsule's LEC had taken place (Shah et al., 2009). The anterior capsule's increased opacification and heightened phymosis in healthy eyes without the polishing of LEC, in patients with an implanted hydrophilic acrylic lens with sharp edged optics, was confirmed by Baile et al (Baile et al., 2012).

In experimental study with artificially induced varying grade zonular defects in pigs eyes, using iris retractors and CTR during surgery for stabilisation of the capsular bag, convincing statistically significant maintenance of the capsular bag's form was established compared with the control group, as well as statistically significant reduced entry of lens core fragments in the vitreous body (Yaguchi et al., 2019). The capsule's tension ring was implanted in most cases prior to phacoemulsification, so that the contour of the capsular bag of the subluxated lens was maintained during surgery, providing a function as a barrier between the eye's anterior and posterior segment and reducing the risk of tearing of the remaining zonule (Cionni & Osher, 1998; Cionni et al., 2003; Georgopoulos et al., 2007; Gimbel et al., 1997; Vasavada et al., 2012a).

The average capsulorrhexis area for research patients was 14.24 mm^2 during surgery, which is markedly smaller than the usual capsulorrhexis area created during an uncomplicated cataract operation, which is usually 5–5.5 mm (Choi et al., 2018; Hayashi et al., 2011; Hayashi & Hayashi, 2005; Kim et al., 2013) in diameter, corresponding to 19.625–23.75 mm^2 area. A small capsulorrhexis area for research patients can be explained by 2 factors –

pronounced lens mobility due to weakened or non-existing zonules (Vanags et al., 2017; Vasavada et al., 2012b) and the surgical technique used in which the iris or capsular hooks (retractors) are attached to the capsulorrhexis (and consequently, the entire lens) edge. According to the author's observations, a small capsulorrhexis provides a smaller attachment angle between the attaching hooks and the surface of the lens' capsule, and, therefore, there is less lens and anterior chamber mobility (fluctuations) during surgery, significantly reducing the risk of rupture to the anterior capsule. A small initial capsulorrhexis is an increased risk factor for contraction of the anterior capsule (Sugimoto et al., 1998), which in combination with zonular weakness can cause marked contraction of the anterior capsule with a deterioration or loss of vision, a change in the location of the IOL and the location angle and late IOL dislocation (Al-Kharashi & Al-Obailan, 2009; Davison, 1993; Hayashi et al., 2001; Hayashi et al., 2011; Kato et al., 2002; Subasi et al., 2019). The approach used in the research when the small initial capsulorrhexis was maintained without enlargement, was based on the use of a CTR and a hydrophobic acrylic IOL with a sharp edge, a combination which reduces the risk of contraction of the anterior capsule (Cionni & Osher, 1998; Corydon et al., 2007; Hayashi & Hayashi, 2005; Jacob et al., 2003; Lee et al., 2001).

In the research by Vasavada et al., in which 46 subluxated lens operations with a varying etiology of subluxation were analysed, a surgical technique with a small initial capsulorrhexis was described, which had been enlarged to a standard size (5–5.5 mm in diameter) by the completion of surgery (Vasavada et al., 2012a). A standard initial capsulorrhexis size was reported in other subluxated lens research groups (Das et al., 2009; Santoro et al., 2003).

In research by Lin et al., with various anterior capsule sizes after surgery on a congenital cataract without the implantation of an IOL, in the group with a very small initial capsulorrhexis, the reduction in its opening area at 1- and 6-

month observation visits was 10.09 mm^2 and 9.08 mm^2, respectively (a reduction by 16.97 % and 25.26 %), compared to the initial 12.16 mm^2. In the group with an average sized capsulorrhexis, the results of the same visits were an initial size of 15.22 mm^2, then 13.43 mm^2 in the 1st month and 12.79 mm^2 in the 6th month, with the percentage reduction being 12.92 % and 15.95 %, respectively. In the group with the largest initial capsulorrhexis (22.92 mm^2), the reduction after 1 month was up to 20.86 mm^2 (8.88 %), and 20.49 mm^2 (10.55 %) 6 months post-surgery (Lin et al., 2015). The capsulorrhexis of the study patients was not enlarged, as the author's view is that this is an additional manipulation which can deepen an already weakened zonular defect or damage preserved zonules, aggravating the post-surgery outcome prognosis in this way.

Phase III study by Price et al., about the use of a CTR in cases of subluxated lenses, established a medium (23 patients) and serious (2 patients) contraction of the anterior capsular opening in a 1-year period in 25 of 224 patients, even though the initial size of the anterior capsular opening was not indicated in the research group (Price et al., 2005), which points to the significance of a CTR in reducing the contraction of the anterior capsule.

The reduction in the average capsulorrhexis area of research group patients was gradual, from 14.24 mm^2 during surgery to 12.13 mm^2 in the 6th month after surgery, with a statistically significant reduction being observed 1 month post-surgery. Kim et al. reported a contraction in the anterior capsule of 18.60–18.99 mm^2 on average during surgery to 16.81–17.75 mm^2 in the 3-month observation period for cataract surgery patients who had an intraocular lens implanted, similar to the ones used in the current study. Overall, the average reduction in the capsulorrhexis field formed 6.76–10.87 % of the size of the initial capsulorrhexis in eyes without pathology (Kim et al., 2013), and similar tendencies in eyes without pathology corresponded to the observations made by Choi et al. (Choi et al., 2018) and Corydon et al. (Corydon et al., 2007). Whereas, as reported by Kato, contraction of the capsulorrhexis in a 9-

month period, reduces by 14 % on average in eyes without pathology (Satoshi Kato et al., 2002).

In a study over a 20-year period by Mönestam on 800 patients who were observed to evaluate the incidence of late IOL dislocation not a single significant reduction of the anterior capsular opening was established, which would have required the undertaking of a Nd:YAG anterior capsular laser discision, even though the size of the anterior capsule was not specially measured intraoperatively or postoperatively (Monestam, 2019). In this study, the reduction in the anterior capsular opening area, dependent on the manufacturer of the implanted IOL, does not differ in a statistically significant way, and is connected with the similarity in the features of the construction, materials and surface of the IOL. The reduction of the capsulorrhexis in the study group, with an implanted *Alcon* lens was 11 % on average, but approximately 16 % for both the *Tecnis* and the *Medicontur*, which does not, however, conform to the trend of greater reductions in the anterior capsular opening in eyes with an implanted *Alcon* lens, than those with a *Tecnis ZCB00*. This type of trend was observed in groups where other eye pathology (excluding a cataract) had not been established (Kahraman et al., 2014), as well as in the overall population group, which also included patients with other eye pathology (Hartman et al., 2018).

The average reduction in the capsulorrhexis area for patients in the research group with traumatic lens subluxation was 18.30 %, compared to 13.10 % in the group without traumas. The study by Cionni et al., which included 46 patients with lens subluxation of varying origin, showed that in comparing traumatic and non-traumatic causes for surgery for lens subluxation with the implantation of a mCTR (Cionni) and hydrophobic acrylic lens, statistically significant types of post-surgery complications were not established between the groups (Vasavada et al., 2012a). In the case report for a patient with a dramatic lens subluxation who had a cornea transplantation in his

anamnesis (DALK), Kandar recorded constancy in the anterior capsular opening, which the author associated with a sufficiently large initial capsulorrhexis (5 mm, conforming to 19.625 mm^2), as well as the implanted mCTR (Cionni) ring and hydrophobic acrylic lens (Kandar, 2014). The reduction of the anterior capsulorrhexis area by 18.30 % in this study could be explained by the smaller initial size of the capsulorrhexis, as a CTR or mCTR (Cionni) in combination with hydrophobic acrylic lenses, were implanted for all patients.

As can be seen in Figure 2.7, a marked reduction in the capsulorrhexis field can be observed for those patients in the research who had a CTR with a diameter of 11 mm implanted, with a reduction of 22.7 % in a 6-month period (13.70 mm^2 to 10.58 mm^2), whereas the reduction with a CTR of 12 mm diameter was 8.07 % (14.61 mm^2 to 13.43 mm^2 in a 6-month period). In the experimental study with pigs' eyes, it was established that a CTR helps in maintaining a relatively unchanging anterior capsulorrhexis and that changes in the capsulorrhexis are not dependent on the diameter of the CTR. For eyes with only an IOL implanted, there were larger differences in the size of the capsulorrhexis opening (Lee et al., 2001).

For patients without other eye pathology, except for cataracts, the reduction in the capsulorrhexis in a 3-month period after cataract surgery with the implantation of a CTR, did not have statistical reliability (Kurz et al., 2006). In the study by Takimoto et al. on IOL centration and the tilt in its position, and changes in the anterior capsular opening for patients with zonular weakness in the CTR group using 2 types of capsular rings with a diameter of 12.3 and 13 mm, statistically significant capsulorrhexis reduction indicators were not found between the two types of rings (Takimoto et al., 2008). The author of this study considers that the diameter of the CTR has a significance, as a larger diameter CTR ensures a more pronounced stretching of the capsular bag, in this way resisting contraction in the capsulorrhexis, which was proved by the difference

between the percentage reduction in the capsulorrhexis between an 11 and 12 mm CTR in the post-surgery observation period. A significantly smaller contraction of the anterior capsule was observed for retinitis pigmentosa patients, who had a CTR implanted, than for the group in which it was not implanted, confirming the significance of a CTR in the reduction of the capsular contraction syndrome, in this way (Bayyoud et al., 2013).

A reduction in the capsulorrhexis of 18.70 % (from 13.90 to 11.30 mm^2) was established for patients in the research who had a CTR implanted, whereas, the reduction in the capsulorrhexis for eyes where a modified CTR (Cionni) had been implanted was 9.01 % (from 14.65–13.33 mm^2), which is also confirmed in the Author's publication (Vanags et al., 2017). As was previously mentioned, the implantation of a CTR after cataract surgery in eyes with no other pathology, did not affect the anterior capsular opening (Kurz et al., 2006; Lee et al., 2001; Tribus et al., 2007), but reduction in the capsulorrhexis in eyes with zonular weakness was small, even though a marked reduction in the anterior capsular opening also could not be excluded in individual cases (Price et al., 2005; Takimoto et al., 2008). PEX syndrome was established more in patients with an implanted CTR, which could explain the marked trend toward a reduction in the capsulorrhexis.

The initial capsulorrhexis area for patients with PEX syndrome was larger than for other patients, but it reached the size of the capsulorrhexis for other patients in the final visit, and as a consequence, the average reduction in the anterior capsular field was larger, even though a convincing statistical significance was not established. An increased contraction of the anterior capsule in the case of PEX syndrome was already described in 1993 in defining anterior capsular contraction syndrome (Davison, 1993). Hayashi et al., established a marked statistically significant reduction in the anterior capsular opening after uncomplicated cataract surgery with the implantation of an *Alcon* hydrophobic acrylic lens, without the implantation of a CTR for PEX patients,

who did not have any other additional eye pathology, excluding PEX glaucoma (Hayashi et al., 1998). The initial diameter of the capsulorrhexis was about 5.5 mm for all patients, including the control group. After 1 year of observation, a reduction in diameter of 22. 3% (from 25.4 to 19.7 mm^2) was established in the PEX group, with a more significant reduction of 17.5 % already being observed 1 month after surgery. Whereas, in the control group (without other eye pathology, excluding cataracts), the reduction in the anterior capsular opening in a 1-year period was 6.7 % (from 26.5 to 24.8 mm^2). A marked anterior capsular contraction developed in 7 of 53 in the PEX group, with the opening reducing to below 10 mm^2. An anterior capsular fibrosis Nd:YAG laser capsulotomy contraction reduction was undertaken for 5 of them, with the average time period being 6.3 months post-surgery (Hayashi et al., 1998).

Shingleton et al. established increased contraction (phymosis) of the anterior capsule in 9 % of 76 patients with pre-operatively determined zonular weakness for PEX syndrome patients, 12 % of 67 patients who had zonular weakness established intra-operatively, who, compared with 2 control groups which included PEX patients without zonular weakness and patients without other eye pathology, were different in a statistically significant way from the control groups (Shingleton et al., 2017). A CTR was implanted in 52 of the pre- and intraoperative diagnosed PEX syndrome patients with zonular weakness, but was not implanted in 91, and, comparing both groups, statistically significant differences were not established in changes to the capsulorrhexis area in the post-surgery period. When compared with the control group, the reduction in the anterior capsular opening was statistically significant for both high risk groups.

Six patients from the preoperative determined zonular weakness group and 2 patients form the intraoperative diagnosed zonular weakness group, required a Nd:YAG capsulotomy to eliminate anterior capsular fibrosis, although the time period when it was required was not shown. This type of

intervention was not necessary in the control group (Shingleton et al., 2017). It should also be separately noted that, according to Shingleton, the comparatively high number of cases (4.2 %) of pseudophacodonesis, anterior capsular contractions, and the decentration and tilt of the IOL in the control group with PEX syndrome without zonular weakness, when compared with the control group, which had no other eye diseases, thereby emphasised the significance of PEX syndrome in the origin of late complications (Shingleton et al., 2017).

In the PEX sub-group with a high risk of anterior capsular phymosis, Hayashi et al. established a statistically significant average reduction in the anterior capsule of 10.5 % in the 1st month, to 25.1 % in the 6th month of observation in patients without a prophylactic Nd:YAG laser discision of the anterior capsule, compared with a 3.4 % reduction in the 1st month and a 13.0 % reduction in the 6th month of observation for the PEX patient group, which had a prophylactic Nd:YAG laser discision of the anterior capsule (Hayashi et al., 2011). A marked contraction of the anterior capsule was not established for any of the PEX syndrome patients with zonular dialysis (7 cases of 106 (120 eyes) for PEX patients with 503 patients in total involved in the research) in the research in north-western Spain, but there is lack of data about CTR use for these (Vazquez-Ferreiro et al., 2019). Borkenstein established anterior capsular opening phymosis in a 10-month observation period for 3 of 15 patients (20 %) with PEX syndrome and zonular weakness, who had surgery on cataracts with the phacoemulsification method without the implantation of a CTR and an implanted hydrophobic acrylic lens (the design is similar to that used in the current study) *(*Borkenstein & Borkenstein, 2019), which is more than for the patients in this study (15.1 %), demonstrating the significant role of a CTR in the reduction of anterior capsular fibrosis, in this way.

A statistically significant reduction in the anterior capsular opening was observed for patients in this research with glaucoma. The data can be explained by the fact that PEX syndrome was also established for the majority of

glaucoma patients, which is also one of the main risk factors for capsular contraction (Alfaiate et al., 1996; Davison, 1993; Hayashi et al., 1998; Hayashi et al., 2011; Shingleton et al., 2017). Hayashi et al. compared anterior capsular contraction after uncomplicated cataract surgery for PEX syndrome and PEX syndrome patients with glaucoma, but statistically significant differences were not established (Hayashi et al., 1998). In the study by Subasi et al. on late dislocation, glaucoma was mentioned as one of the factors which predisposes late IOL dislocation, and was established in 6 of 39 patients involved in the study, with 5 of them also having PEX syndrome (Subasi et al., 2019).

Consequently, glaucoma could be a significant factor in increased capsular contraction. Ostern et al. explain glaucoma as a risk factor for late IOL dislocation as a by-effect of late stage PEX syndrome (Ostern et al., 2014), which also confirms the findings in the current study, where glaucoma patients had a greater reduction in the anterior capsular opening, where the majority of the glaucoma patients also had PEX syndrome.

Myopia was already mentioned in early publications as one of the reasons for increased contraction of the anterior capsule due to zonular weakness (Davison, 1993). This was established for 6 patients or 11.6 % in the research. Chinese study which was published in 2018, which included 38 eyes of 19 patients with an axial eye length > 27 mm and with eyes being defined as having extreme myopia with zonular weakness and on which cataract surgery had been undertaken with the phacoemulsification method with (1^{st} group) or without (2^{nd} group) polishing of the anterior capsule of LEC, the greatest contraction of the anterior capsule was 1 month post-surgery in both groups with contraction reducing evenly up to the 6^{th} month without the observation of a statistically significant reduction between the groups; a CTR was not implanted in any patient, and marked anterior capsular fibrosis, which would require Nd:YAG laser capsulotomy, was also not established.

In the 1st group, the reduction in the anterior capsular area was from 25.26 mm^2 on the 1st day post-surgery, to 23.97 mm^2 1 month post-surgery and 23.26 mm^2 6 months post-surgery, which constitute 5.1 % and 7.91 %, respectively. In the 2nd group, the initial capsulorrhexis was 25.46 mm^2, which reduced in the first month to 23.78 mm^2, in the 6th month – to 2.64 mm^2, with the percentage reduction in the 1st and 6th month being 6.59 % and 11.07 %, respectively (Wang et al., 2018).

Anterior capsular contraction syndrome in a case of serious myopia could be explained by an increased quantity of TGFβ2 in the anterior chamber fluid, which after cataract surgery provides additional stimulation for the transformation of LEC into myofibroblasts (Zhu et al., 2016); whereas in the case of congenital lens ectopia, or subluxation, the increase in TGFβ2 in the anterior chamber's fluid, correlated with an increased stage of lens subluxation (Cao et al., 2019) As a consequence, in the case of myopia, increased capsular contraction is like a manifestation of weakened or non-existent zonules. Marked capsular contraction in both eyes after cataract surgery for a patient with serious myopia without the implantation of a capsular tension ring was reported in case reports (Xiao et al., 2011; Zhang et al., 2012), even though this was noted to be a rare complication – 1 in 54 patients with serious myopia, post-cataract surgery (Xiao et al., 2011).

In the period from 2011 (commencement of the study) to January 2020, late IOL-CTR-capsular bag dislocation was observed for 7 patients (13.2 %)(Vanags et al., 2021). Mönestam recorded 1.2 % late IOL dislocation in a 20-year period for a group of 800 cataract patients who had surgery from 1997–1998, of whom 39 % had PEX syndrome, and for all patients with late IOL dislocation, it was observed as a complex dislocation of the IOL-capsular bag, and there were no cases of a separate IOL dislocation with the capsular bag remaining unaffected (Monestam, 2019). Mönestam's study group also included 11 patients with a CTR implanted during surgery, which provided

evidence of zonular weakness or lens subluxation, but late IOL-CTR-capsular bag dislocation developed for 18 % (2) of the patients in these subgroups (Monestam, 2019), which is more than for patients in the current research group, even though the observation period in Mönestam's research was also significantly larger.

Consequently, the increase in the number of late dislocations can be expected to be greater in the future. This is also confirmed by Mönestam's combined study group's late IOL dislocation time frame, from the initial cataract surgery to the IOL dislocation, and this ranges from 3 years and 9 months to 19 years. The late dislocation period was not indicated for patients who had a CTR implanted (Monestam, 2019), but in any case, the first cases of late IOL-CTR-capsular bag dislocation in this study were already observed 1, 2 and 3 years after the initial surgery (Vanags et al., 2021; Vanags & Laganovska, 2020), which is earlier than in Mönestam's study.

In the study by Bayyoud et al. with 46 patients who were suffering from retinitis pigmentosa and had cataract surgery with the implantation of a hydrophobic acrylic lens with or without the implantation of a CTR, late IOL dislocation in both eyes was established for 1 patient (from the group in which the CTR had not been implanted) in the 8-year observation period, although a precise dislocation time was indicated (Bayyoud et al., 2013). In retrospective study conducted in Lithuania in 2013, the average time for a late IOL-capsular bag dislocation was 67 months post-cataract surgery, with the greatest risk factor being mentioned as PEX syndrome (56.9 %), intra-operatively established zonular weakness (35.3 %), CTR implantation (29.4 %), and trauma (21.6 %) (Krepste et al., 2013).

Research by Das et al. with CTR implantation in children, established late IOL-CTR-capsular bag dislocation for patients with MS 2 years after initial surgery, indicating progressive zonular weakness and increased anterior capsule contraction as the possible reason (Das et al., 2009). It should be noted that

patients had a hydrophilic acrylic lens implanted, which increases the possibility of anterior capsular contraction (Zemaitiene et al., 2008). Gunenac et al. reported 2 cases of IOL-CTR-capsular bag late dislocations 6 years after the initial surgery, as well as indicating a simple operation with a low risk of complications associated with repositioning of the IOL-CTR-capsular bag – a complex *sulcus* attachment at 12.00 position with a polypropylene suture, attaching this to the edge of the CTR (Gunenc et al., 2014), with the Author of the current study using a similar approach (Vanags & Laganovska, 2020). Analysis of 3 cases by Kocak et al. revealed a late IOL-CTR-capsular bag dislocation 2.5 years, 3 years un 8 years post-cataract surgery for patients with zonular weakness, which were associated with PEX syndrome, with all patients having a characteristic marked fibrotic anterior capsular opening with a fibrotic capsular bag, with the implanted IOL material being hydrophilic acrylic (Kocak et al., 2017).

Decentring of the IOL in PEX patients over a 3-month post-surgery period was established in 6.5 % of patients in research conducted in Portugal (Alfaiate et al., 1996), but with good visual acuity being preserved, and, therefore, repositioning or lens exchange surgery was not undertaken. Shingleton et al. observed late IOL dislocation in 3 patients of 143 in high risk groups (PEX patients with preoperative or intraoperative diagnosed zonular weakness), although it was not separately shown whether these patients had a CTR implanted, and in the control group – late IOL dislocation was established in 1 patient of 76 with PEX syndrome, without signs of zonular weakness (Shingleton et al., 2017).

This study also showed that there were no statistical differences between patients, who had or did not have a CTR implanted in relation to high numbers of late complications (including late IOL dislocations) in risk groups (Shingleton et al., 2017). In the Indian state of West Bengal, IOL decentration was observed in 23 of 512 PEX syndrome patients in a 3-month post-surgery

period, which the authors associate with zonular weakness or lens subluxation (Islam et al., 2017).

Late IOL-CTR-capsular bag dislocation took place for 1 of the study patients, as a result of the tearing of the attachment suture 2 years after initial surgery (a mCTR (Cionni) had been implanted). This period corresponds with the average tearing time of the 10/0 polypropylene attachment (17.84 months) in the study conducted by Cionni et al. with 90 eyes of 57 patients with lens subluxation caused by various congenital pathologies, while late IOL-CTR-capsular bag dislocation was also established in 9 eyes (10 %) (Cionni et al., 2003).

Late IOL-CTR-capsular bag dislocation in patients with an implanted mCTR (Cionni) to correct lens subluxation of posttraumatic origin, which had been attached with a 9/0 polypropylene thread, was established 6 years after traumatic cataract surgery, with the reason being the tearing of the polypropylene thread, with the case being resolved by attaching the Cionni ring again with 9/0 polypropylene thread (Cheung et al., 2018).

Laser discision of the anterior capsule to eliminate marked capsular fibrosis (phymosis) was undertaken for 15.1 % (8 of 53) of study patients, 4 with PEX syndrome(Vanags et al., 2021). The average reduction in the anterior capsular opening for these patients over a 6-month period was 32.6 % (13.46 mm^2 to 9.06 mm^2). Hayashi et al. described a more marked reduction in the anterior capsular opening for PEX syndrome patients, for 9.4 % of whom the anterior capsular opening area was reduced to below 10 mm^2 in a 12-month period post-cataract surgery, which is why a Nd:YAG anterior laser discision was undertaken for these patients (Hayashi et al., 1998).

Ye et al. analysed 11 patients with phymosis of the anterior capsular opening, and the average time that a Nd:YAG anterior laser discision undertaken was 4.4 ± 1.4 months. The diameter of the anterior capsular opening prior to the laser discision was 2.2 ± 0.8 mm (or 3.8 ± 0.5 mm^2), progressive

zonular weakness was observed in 2 patients, but late IOL dislocation was not observed during the period of the study (Ye et al., 2018). 9 of the 11 patients had at least one high risk factor for increased anterior capsular contraction (diabetes mellitus, high myopia or retinitis pigmentosa) (Bayyoud et al., 2013; Hayashi et al., 2011; Xiao et al., 2011).

In the present study, 2 patients (N21 and N26) with early anterior capsular phymosis and Nd:YAG anterior laser discision (in the 2nd month for N21 and the 1st month for patient N26) had IOL-CTR-capsular bag dislocation, 3 and 7 years after cataract surgery, respectively, and these facts could indicate that an early and marked reduction in the anterior capsular opening is an additional risk factor in late IOL dislocation.

A persuasive connection was not found in the study between a reduction in the anterior capsular opening and the time of surgery in either the study or the control group, Although, taking into account the time of, which is longer than for the control group, and the additional instruments used, which mechanically irritate the uveal tissue (iris retractors, CTR and mCTR), the reaction to the inflammation with its consequently greater contraction of the capsular opening should have been greater for patients with lengthier surgery.

In a study with rabbits' eyes, in which IL-1 receptor antagonists were introduced, fewer post-operative inflammation indicators were established compared to the control group, and in the 6-month observation visit, markedly fewer capsular fibrosis IL-1 receptor antagonists were established in the rabbits' eyes which received them, compared with the control group. This indicates the stimulatory significance of an inflammation mediator (in this case IL-1) in the transformation of LEC into myofibroblasts (Nishi et al., 1994).

In cases of phacoemulsification, an opening was created in the anterior capsule of the lens, breaking down the natural barrier between inflammation mediators and the LEC in this way, which is why the regenerative mechanisms in the LEC receive enhanced stimulation for their transformation into

myofibroblasts, which is facilitated by inflammation mediators (MCP-1, IL, TNF-α, TGF-β, VEGF) (Kawai et al., 2012; Zhu et al., 2016). The inhibiting of MMP, the levels of which increase in cases of inflammation, also significantly decreased proliferation of LEC and capsular contraction in the study with cell cultures exhibited in the lens capsules of human corpses (Wong et al., 2004).

Increased reduction in the anterior capsular opening, as a response to extended increased inflammatory reaction as a result of a break-down of blood-aqueous humour barrier was reported in the study, in which data for patients with diabetes mellitus was analysed (Kato et al., 2001), with this barrier being mechanically influenced in the study group, as the iris is often irritated by iris retractors, as well as for a large group of patients with PEX syndrome group, for whom increased permeability of the blood-aqueous barrier is part of the syndrome (Hayashi et al., 2011; Kanthan et al., 2013).

Hayashi et al. (Hayashi et al., 2013) compared PEX syndrome patients after uncomplicated cataract surgery with the control group, but did not establish statistically significant signs (flares) of anterior chamber inflammation between the groups, even though it was slightly larger in the PEX group. Shah et al. (Shah et al., 2009), in analysing the reaction to anterior chamber inflammation in cataract patients after additional 5 minute polishing of the anterior capsule's LEC, found a marked increase in the number of inflammatory cells and flares, compared with the control group, which indicated that there is an increase in the growth of inflammatory reaction with an additional period of manipulation.

Conclusions

1. The reduction of the anterior capsular opening after cataract surgery for patients with a subluxated lens is gradual, with the most rapid reduction 1 month post-surgery.
2. A prediction model has been developed for the capsulorrhexis area 3 month post-surgery value which allows for the more accurate identification of patients with a greater risk of rapid reduction in the capsulorrhexis.
3. Postoperative and late complications are observed more for patients with pseudoexfoliation syndrome and glaucoma. Late IOL-CTR-capsular bag dislocation in the subluxated lens group can often be encountered, but its development period in the long-term post-operation period does not differ from the time for late IOL dislocation patients after non-complicated cataract surgery. Zonular weakness/absence, a small initial capsulorrhexis and the non-polishing of the anterior capsule's LEC does not influence the size of the contraction of the anterior capsule, if a CTR or a modified CTR and a hydrophobic acrylic IOL are used in the surgery.
4. The use of a capsular tension ring or a modified capsular tension ring reduces the contraction of the anterior capsule opening significantly over time, with the size of the contraction being comparable to the case of a non-complicated cataract surgery. Zonular weakness/absence, a small initial capsulorrhexis and the non-polishing of the anterior capsule's LEC does not influence the size of the contraction of the anterior capsule, if a CTR or a modified CTR and a hydrophobic acrylic IOL are used in the surgery.
5. Subluxated lens cataract surgery can be compared to standard cataract surgery, using additional instruments and devices (iris and capsular

hooks, a CTR or mCTR) for lens and capsular bag stabilisation, zonular conservation and stabilisation, so as not to deepen the defect.

6. Recommendations have been developed for surgical tactics in the treatment of subluxated lenses to reduce postoperative and late complication risks.

Practical recommendations

1. Subluxated lens surgery should be undertaken by the phacoemulsification method, using iris or capsular retractors for the stabilisation of the lens capsular bag and lenses, implanting a CTR or a modified CTR in the capsular bag, and implanting a hydrophobic acrylic IOL in the capsular bag.
2. The subluxated lens surgical tactics diagram at Attachment No. 4 should be used in deciding the tactics for subluxated lens surgical treatment.
3. More frequent post-surgery visits are recommended for patients after subluxated lens surgery for the early diagnosis of later complications.
4. Using the anterior capsular opening's 3-month prediction model, undertake observation of the anterior capsule's Nd:YAG laser discision's marked phymosis early in the (up to the 1st month) post-surgery period, to reduce the risk of late IOL-CTR-capsular bag dislocation.

Future research directions

1. Research the capsulorrhexis area in relation to cultivation of samples of the anterior capsule obtained during surgery in a cell culture, and its contraction/fibrosis depending on the effect of growth factors in various concentrations, and including the results in the anterior capsular opening's reduction 3-month model.
2. Analysis of the concentration of the biologically active substance (TGF-beta2) in the anterior chamber fluid and its relationship with the contraction of the anterior capsular opening, and the frequency of the late dislocation of the IOL-CTR-capsular bag.
3. A long-term cost effectiveness analysis, comparing the methods included in this study with a pars plana lentectomy and IOL implantation in the anterior or posterior chamber with one of the methods which is not connected with its implantation in the lens capsular bag.
4. Comparing the differences in the late results between the approach used for the observation of patients in the research with a group where the anterior capsular opening reduction 3-month model has been used in analysis and selection of the direction of therapy.
5. Comparing the effect of an early and late Nd:YAG anterior laser capsulotomy on the condition of zonules after subluxated lens cataract operations.

Publications and reports about the theme of the thesis

Publications

1. **Vanags, J.**; Erts, R.; Laganovska, G. Anterior capsule opening contraction and late intraocular lens dislocation after cataract surgery in patients with weak or partially absent zonular support. *Medicina (Kaunas)* 2021; *57*, 35. doi: 10.3390/medicina57010035
2. **Vanags J**., Laganovska G. "Long-term outcome of cataract surgery in eyes with pseudoexfoliation syndrome associated with weak zonules: a case report." *Case Reports in Ophthalmology*. 2020; 11(1): 54–59. doi:10.1159/000505720
3. **Vanags J**., Erts R., Laganovska G. "Anterior capsulorrhexis opening reduction after cataract surgery with subluxated lenses." *Medicina (Kaunas)*. 2017; 53(5): 310–315. doi:10.1016/j.medici.2017.10.003
4. Valeina S., Sepetiene S., Laganovska G., Radecka L., **Vanags J**., Erts R., Meskovska Z., Sture E. A. "Analysis of Vision Development in Patients after Childhood Cataract Surgery." *Acta Chirurgica Latviensis*, 2015 (15/1), 12–17.
5. Valeina S., Heede S., Erts R., Sepetiene S., Skaistkalne E., Radecka L., **Vanags J**., Laganovska G. "Factors influencing myopic shift in children after intraocular lens 98 implantation." European Journal of Ophthalmology, EJO-D-18-00722R1 26:1120672119845228. doi: 10.1177/1120672119845228.

Reports at conferences

International conference thesis

1. **Vanags J**., Laganovska G. "Structure and visual outcomes of reposition operations of late Intraocular lens(IOL) dislocation", XIV Forum Ophthalmologicum Balticum 2013., Abstract book, p.61, 2013. 23–24 March, thesis and oral presentation
2. **Vanags J**., Baumane K., Laganovska G. "Keratometric changes after subluxated lens cataract surgery", ESCRS 2013, POS-2963, thesis and poster presentation

3. **Vanags J**., Laganovska G. “Surgical management of subluxated lens in Latvia.” Forum Ophthalmologicum Balticum XV, 2016. 20 August, Abstract, p. 40, thesis and oral presentation
4. **Vanags J**., Laganovska G. “Intraocular pressure changes after subluxated lens surgery by means of cionni ring implantation or iol iris-fixation”, DOG 2014, Abstract No. 650, thesis and poster presentation
5. **Vanags J**. “Lens subluxation after blunt trauma”, BEST Vol. 2 Ocular Trauma Summit, Vilnius 2014, oral presentation
6. **Vanags J**., Laganovska G. “Analysis of operative treatment of lens dislocation secondary glaucoma”. XIII Forum Ophthalmologicum Balticum, O-13, Abstract book, Vilnius 20–22 August, 2010, p. 35, thesis and oral presentation
7. Laganovska G., **Vanags J**. “Postoperative results and complications of cataract surgery in cases of traumatic lens dislocation.” XXVIII Congress of ESCRS, p.114, Paris 2010, thesis
8. Laganovska G., **Vanags J**. “Surgical management of dislocated lenses”. Paedriac Ophthalmology Congress, Rīga, 2011, Abstract book, p. 203, thesis
9. **Vanags J.**, Sproģis Ē., Laganovska G. “Influence of stage of lens subluxation on surgery time”, 40th Nordic Congress of Ophthalmology, Abstract Su-No4-2, 24–28 August, 2012., thesis and oral presentation.
10. Rasčevskis D., Balode A., **Vanags J**., Laganovska G. “Anterior capsule opening contraction after vitreoretinal plus cataract surgery”, 24th ESCRS winter meeting, 2020, thesis.

Latvian conference thesis

1. **Vanags J**., Baumane K., Laganovska G. “Keratometrisko mērījumu izmaiņas pēc subluksētu lēcu operācijām” (Eng. Changes in keratometric measurements after subluxative lens operations), RSU Academic Conference, 10 April, 2014, p. 45., thesis and oral presentation
2. Valeiņa S., Laganovska G., Radecka L., **Vanags J**., Erts R. “Salīdzinošs redzes attīstības novērtējums pacientiem ar operētu iedzimto kataraktu atkarībā no kataraktas morfoloģiskā tipa, attīstības sākuma laika, implantētās IOL mērķa stipruma un pēcoperācijas komplikācijām” (Eng. Comparative assessment of visual development in patients with operated congenital cataracts depending on the

morphological type of the cataract, the time of onset of development, the strength of the implanted IOL target and postoperative complications), RSU 2014 Academic Conference thesis, p. 227.

3. **Vanags J**., Laganovska G. "Retrospektīva dislocētu lēcu operāciju rezultātu analīze" (Eng. Retrospective analysis of the results of dislocated lens operations), RSU 2010. Academic Conference thesis, RSU, 18–19 March, 2010, p. 62, thesis and oral presentation
4. **Vanags J**., Sproģis Ē., Laganovska G. "Pēcoperācijas rezultāti atkarībā no intraokulārās lēcas (IOL) centrējuma subluksētu lēcu gadījumos" (Eng. Postoperative results depending on intraocular lens (IOL) centering in subluxative lenses), RSU 2012 Academic Conference thesis, RSU, 29–30 March, 2012, p. 42, thesis and oral presentation
5. Rasčevkis D., Balode A., **Vanags J**., Laganovska G. "IOL dislocation after vitreoretinal plus phaco surgery depending on capsulorhexis size and overlap" RSU Academic Conference 2019, p. 470, thesis

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