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Macula Translocation in Age-related Neovascular disease

Surgical Management of Subfoveal Choroidal Neovascular Membranes in Age-Related Macular Degeneration by Macular Translocation (MARAN)

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Macula Translocation in Age-related Neovascular disease Surgical Management of Subfoveal Choroidal Neovascular Membranes in Age-Related Macular Degeneration by Macular Translocation (MARAN)

Biometrical Report

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Abbreviations

AE:	Adverse event
ARMD:	Age-related macular degeneration
CNV:	Choroidal neovascularization
ETDRS:	Early treatment diabetic retinopathy study
ITT:	Intention to treat
KKS:	Coordination Center for Clinical Trials
LOCS:	Lens Opacities Classification System
MT:	Treatment group (Macular Translocation surgery)
PED:	Pigment epithelial detachment
PDT:	Photodynamic Therapy
PVR:	Proliferative vitreoretinopathy
RPE:	Retinal pigment epithelium
SAE:	Serious adverse event
ST:	Control group (Standard Therapy)
TTT:	Transpupillary Thermotherapy

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1 Introduction and Objective of the Trial

Age-related macular degeneration (ARMD) is the most common cause of legal blindness in the western countries. Loss of central visual acuity is secondary to submacular atrophy of retinal pigment epithelium and choroidal neovascularization (CNV). Only a small minority of patients with subfoveal CNV can be allocated to conventional laser therapy. At the planning phase of the MARAN trial, no therapeutic regimen was available for the large majority of patients with occult subfoveal CNV (70% of eyes with exudative type of CNV) and geographic atrophy to prevent the loss of central vision in ARMD. Results from recent trials are presented in Süsskind et al. (2007), Lüke et al. (2007), and Gelisken et al. (2007).

Pilot data from laboratory and clinical studies indicate that central visual acuity can be stabilized and partly improved by new surgical strategies. In macular translocation, the fovea is rotated to an area of intact RPE, choriocapillaris and Bruch´s membrane adjacent to the subretinal defect.

The MARAN trial (**Ma**cula-T**r**anslocation in **A**ge-related **N**eovascular disease) aimed at evaluating the efficacy of a new surgical approach in patients with clinical signs and symptoms of exudative ARMD with CNV. Information about the MARAN trial is available at The National Research Register under N0207150031.

In the first phase of the trial (taking until July 2005), biostatistics, monitoring and data management were performed at the Coordination Centre for Clinical Trials, University Hospital Heidelberg. The trial was planned and designed by Kristina Unnebrink (formerly: Coordination Centre for Clinical Trials, University Hospital Heidelberg). In the second phase (since July 2005), the responsibility for biostatistics and data management was carried over from the Coordination Centre for Clinical Trials to the Institute of Medical Biometry and Informatics (IMBI), Heidelberg University. From that time on, the MARAN trial has been performed as common project between the IMBI and the Institute of Biometry and Bioinformatics, Medical School, LMU Munich (IBE). Prof. Dr. Ulrich Mansmann (chair of Biometry and Bioinformatics (IBE)) is the leader and also the responsible of the AMD project. The trial was founded by the German Research Foundation (DFG), Grant MA 1723/1-1.

2 Design of the Trial

2.1 Trial Plan

The study was designed as a multicenter, prospective, randomized (1:1) clinical trial with two groups:

- Treatment group (***MT*** group): in these patients, the ***M***acular ***T***ranslocation surgery was performed.
- Control group (***ST*** group): in these patients, the following options concerning the ***S***tandard ***T***herapy were performed: the observation of the natural course or performing the established treatment in case of progressive cataract, subretinal hemorrhage, or transition of the initial occult membrane to a predominantly classical membrane.

The therapeutical outcome of surgical macular translocation was evaluated in comparison to the spontaneous course or to established treatments in case of the above mentioned circumstances. The main objective was to investigate the efficacy of macular translocation to preserve and improve vision in ARMD. The primary

endpoint was the change of visual acuity (ETDRS) at week 52 after randomization, compared to initial visual acuity. The secondary endpoints were the change in

- reading performance
- contrast sensitivity
- stability of fixation
- eye specific quality of life
- absolute number of letters read correctly

at week 52 after randomization, compared to entry examination.

Figure 1 shows the time course of treatment and observation of one patient within the MARAN trial:

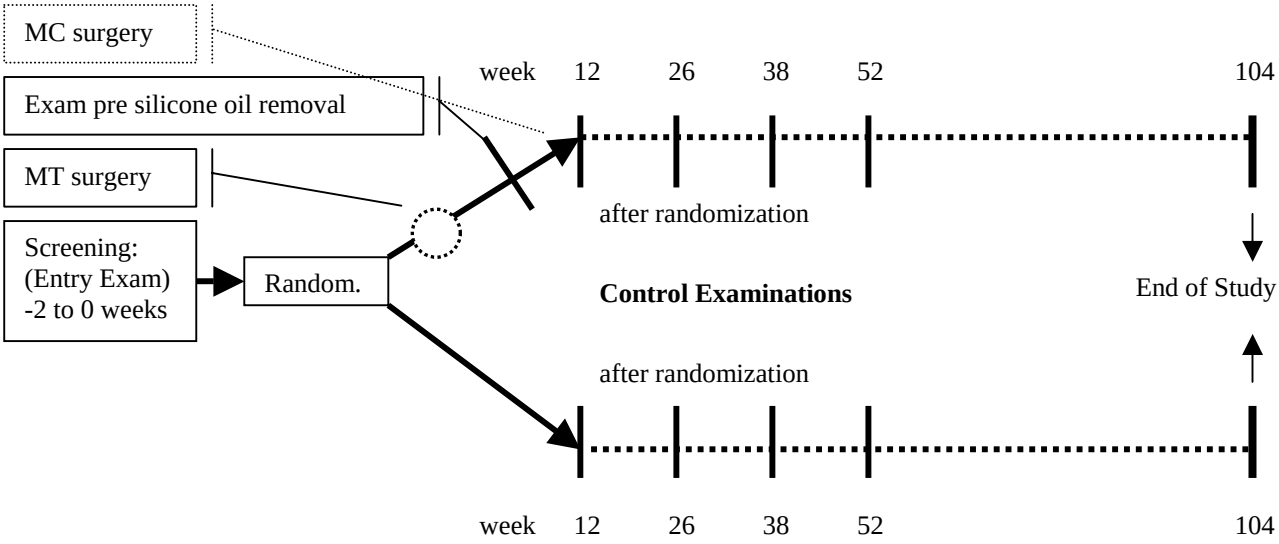

Figure 1: Overview and time course of the MARAN trial (Exam: Examination, Random.: Randomization, MT surgery: Macular Translocation surgery, MC surgery: muscular counterrotation surgery).

A time schedule of all examinations is shown in Table 1. Criteria for the evaluation of the primary endpoint are marked in bold and italic style (X).

Table 1: Data acquisition and time schedule of examination: SO = Silicone Oil.

Parameters, documentation	Screening	Pre SO removal (only treated eyes)	Control examinations after randomization				
Time (weeks after/before randomization)	- 2 to 0	4-12	12	26	38	52	104
Inclusion and exclusion criteria	X						
Consent	X						
Medical history	X						
Adverse events/Serious adverse events		X	X	X	X	X	X
Visual acuity (ETDRS)	***X***	X	X	X	X	***X***	X
Reading performance/speed (Radner)	X		X	X	X	X	X
Contrast sensivity	X		X	X	X	X	X
Slitlamp examination	X	X	X	X	X	X	X
Tonometry	X	X	X	X	X	X	X
Grading of cataract (LOCS 3 illuminated)	X		X	X	X	X	X
Cyclorotation and binocularity	X	X	X	X	X	X	X
Goldmann perimetry	X					X	X
Classification (funduscopy)	X		X	X	X	X	X
Photography (fundus)	X		X	X	X	X	X
Angiography (Fluorescein)	X		X	X	X	X	X
Quality of life	X			X		X	X
Motility assessment, only treated eyes	X	X	X	X		X	X
Low vision aids evaluation			X			X	
End of study							X

Recruitment of patients was planned in the following sites: University Hospital Cologne (Eye Clinic), Rheinisch Westfälische Technische Hochschule Aachen (Department of Ophthalmology), St.Fransziskus Hospital Münster (Eye Clinic), University Hospital Essen (Eye Clinic), University Hospital Tübingen (Eye Clinic I), University Hospital Kiel (Eye Clinic), University Hospital Bonn (Eye Clinic), University Hospital Würzburg (Eye Clinic), Duke University Durham (Eye Center), Royal Liverpool University Hospital (Eye Clinic), Osaka Medical School (Department of Ophthalmology).

2.2 Study Entry Committee

The participating surgeons head to provide proof of skill in order to reduce the effect of learning on study outcome. Before the study started, the study entry committee (Prof. Dr. B. Kirchhof, Prof. Dr. U. Bartz-Schmidt, Dr. K. Unnebrink) evaluated each surgeon in every trial site to verify sufficient surgical skills. The evaluations were made using patient charts of at least 10 current consecutive eyes of macular translocation surgery per surgeon for rate of PVR, retinal detachments and other adverse effects from macular translocation surgery. Each patient should have a minimum follow-up of 3 months after silicone oil removal. A surgeon was admitted to participate in the MARAN trial if he/she could demonstrate a PVR rate, which

upper limit of the 80% confidence interval was below 40% in this case series. Any retinal detachment under silicone oil or after removal of silicone oil was considered as a complication of PVR, even when periretinal membranes were not apparent at that time.

2.3 Patients

This trial was planned for adults with clinical signs of exudative ARMD with subfoveal choroidal neovascularization. Patients could be recruited, irrespective of sex, if they fulfilled the following criteria (the visual acuity is expressed as decimal equivalent):

- Age: 50 years or older
- Exudative ARMD with purely occult or mixed (classic component<50%) CNV
- The largest distance from the center of the fovea to the superior edge of the area of the lesion in the fluorescein angiogram must not exceed 2500 µm and to the inferior edge not more than 1500 µm allowing sufficient rotation of the foveal center to clinically uneffected RPE
- Phakia, Pseudophakia
- Visual acuity (ETDRS) of the better eye (study eye) between 0.16 (20/125)and 0.34 (20/60)
- Visual acuity (ETDRS) of the poorer seeing eye (fellow eye) 0.1 (20/200) or less
- Symptoms: Recent loss of reading ability (newsprint) no longer than 4 months (maximum optical addition for reading glasses is plus 3.00 dptr.)
- Evidence of ARMD in the fellow eye
- Agreement of the patient on follow-up of two years
- Written consent of the patient
- Sufficient lag time after participation in another clinical trial (more than 3 months)
- Absence of severe systemic diseases and inability to have general anesthesia.

The participation in this trial was disallowed if one or more of the following exclusion criteria were applicable:

- 100 % serous Pigment Epithelium Detachment (PED)
- Additional ocular diseases reducing the visual acuity: diabetic retinopathy, retinal artery or vein occlusion, glaucoma in a late stage, uveitis
- Previous laser photocoagulation or PDT, TTT for CNV in the study eye
- Previous ocular radiation therapy in the study eye
- Previous antiangiogenic therapy, e.g. interferon
- Participation in another clinical trial
- Inability to understand the rationale of this trial or the study aim
- Aphakia
- Systemic corticosteroid or other immuno-modulating treatment.

In order to clarify the inclusion and exclusion criteria, the study protocol was amended on October 11, 2002 and October 1, 2003 (Amendment 3 and Amendment 4, see part 2.6.6). The following changes in the inclusion criteria and exclusion criteria were made:

Amendment 3:

Replacing the second inclusion criterion:

- Exudative ARMD with purely occult or mixed (classic component<50%) CNV

with

- Exudative ARMD with subfoveal lesion. CNV must be occult or mixed (classic component < 50%) CNV with or without concurrent pigment epithelial detachment.

Deletion of the first exclusion criterion without any replacement:

- 100% serous Pigment Epithelium Detachment (PED)

and addition of the following exclusion criteria:

- Any subfoveal bleeding
- Chorioretinal anastomoses.

Amendment 4:

Inclusion criteria were modified in the following way:

Patients can be recruited, irrespective of sex, if they fulfill the following criteria:

- Age: 50 years or older
- Exudative ARMD with subfoveal lesion. CNV can be either classic, occult, or mixed (classic component < 50%) CNV with or without concurrent pigment epithelial detachment and bleeding, as long as the total leason size is no larger than 2 times the size of the membrane itself
- The largest distance from the center of the fovea to the superior edge of the area of the lesion in the fluorescein angiogram must not exceed 2500 µm and to the inferior edge not more than 1500 µm allowing sufficient rotation of the foveal center to clinically uneffected RPE
- Phakia, Pseudophakia
- Visual acuity (ETDRS) of the better eye (study eye) between 0.05 (20/400) and 0.34 (20/60)
- Visual acuity (ETDRS) of the poorer seeing eye (fellow eye) 0.1 or less (< 20/200)
- Symptoms: Recent loss of reading ability (newsprint) no longer than 3 months (maximum optical addition for reading glasses is plus 3.00 dptr.)
- Evidence of ARMD in the fellow eye
- Agreement of the patient on follow-up of two years
- Written consent of the patient
- Sufficient lag time after participation in another clinical trial (more than 3 months)
- Absence of severe systemic diseases
- Ability to have general anesthesia.

Exclusion criteria were replaced in the following way:

Patients cannot be recruited if one the following excluding criteria are applicable:

- Massive subretinal hemorrhage (if the lesion is hidden behind the blood and cannot be assessed)
- Serous PED (total leason size is larger than 2 times the size of the membrane itself)
- Chorioretinal anastomoses

- Additional ocular diseases reducing the visual acuity: diabetic retinopathy, retinal artery or vein occlusion, glaucoma in a late stage, uveitis
- Previous treatment of the study eye for ARMD (e.g. laser photocoagulation or PDT, TTT, radiation or antiangiogenic therapy)
- Participation in another clinical trial
- Inability to understand the rationale of this trial or the study aim
- Aphakia
- Systemic corticosteroid or other immunomodulating treatment.

Thus, three versions of page 17 of the CRF were applied in the MARAN trial (see part 3.1).

In order to assess the eligibility for participation on the MARAN trial, at the screening, a photography of the fundus as well as fluorescein and Indocyanine green angiography were performed. Digital files of these photographs were sent to the angiography reading center to decide about the eligibility.

2.4 Course of the Trial

The trial consists of the four parts Screening (entry examination), Randomization, Treatment, and Follow-Up Phase, which are characterized in the following.

2.4.1 Screening

In order to check eligibility, the screening must be finished before the randomization. The difference between the date of the entry examination the date of randomization should not exceed two weeks.

2.4.2 Randomization

All patients of the participating sites were randomized by e-mail maran@kks-hd.de at the Coordination Center for Clinical Trials, University Hospital Heidelberg (KKS Heidelberg). The randomization was performed as block-randomization (block length: 6) for the trial site as stratification parameter.

2.4.3 Treatment

Entry examination and start of the treatment must not be more than 14 days apart. The treatment in the MT group consists in macular translocation and phacoemulsification of the lens and posterior chamber lens implantation. As this trial was limited to patients with predominantly occult neovascular membranes, alternative treatment such as solitary surgical membrane excision was not applicable due to large surgically-induced defects leading to a lack of central fixation. According to the MPS Study (Macular Photocoagulation Study Group 1982, 1986a, 1986b, 1991a, 1991b) and the TAP 1 Study (TAP study group (1999)), there was also no other treatment recommendation. Therefore, observation or approved treatment in cases of a change of the appearance of the neovascular disease served as control.

Patients randomized to the ST group received no surgical treatment, however, they received the current standard treatment. Current standard therapy was defined as treatment based on the available evidence

accepted by ophthalmologists and the funding agencies of national governments and insurance companies. The following definitions of standard therapy were used

classic (100%) CNV:	PDT
predominantly classic (>= 50%) CNV:	PDT
minimal classic (<50 %) CNV:	no standard
occult CNV with no classic CNV:	if CNV <= 4DA or visual acuity <=0.4: PDT; otherwise no standard.

PDT should be used if applicable according to the current standard therapy; it could be used according to the investigators preference in cases where no standard treatment was established (off-label use).

It was specified in the trial protocol that all patients randomized to the ST group should be observed and documented according to the same protocol as the MT group. All patients were evaluated for low-vision aids.

2.4.4 Control Examinations, Final Examination

Control examinations were planned after 12, 26, 38 and 52 weeks after randomization. The final examination was planned at week 104 after randomization (see Figure 1). The particular tests are shown in the time schedule in Table 1. Additionally, a control examination was performed in the MT group after macular translocation surgery before silicone oil removal.

2.5 Primary and Secondary Endpoints

The main objective of the MARAN trial is to investigate the efficacy of macular translocation surgery to preserve and improve the vision in patients with clinical signs and symptoms of exudative ARMD with CNV.

The *primary endpoint* is the *change in visual acuity* (ETDRS) in the study eye, measured at week 52 after randomization, comparing the visual acuity at the entry examination. The visual acuity was measured with the use of reading charts. These charts contain 14 lines, each with 5 letters, which have to be read at a distance of 4 meters. The visual acuity is defined as number of lines with at least 4 letters read on the ETDRS charts. Details of the measuring procedure are mentioned in part 3.4.2 of the study protocol. In contrast to the study protocol, the visual acuity and the difference in visual acuity is expressed in logMAR (see page 47 of the study protocol) instead of the number of lines read on the EDTRS chart. According to the study protocol, it was intended to evaluate the visual acuity at week 52 after randomization by an independent examiner.

The differences in the following five criteria are regarded as *secondary endpoints* (each measured at 52 weeks after randomization compared to the entry examination):

1. Reading performance of the study eye. The reading performance is evaluated in logMAR for a testing distance of 25cm. According to the study protocol, the testing distance was 40cm for the English version of

the reading chart used in the trial site Liverpool. For data analysis, these logMAR values were corrected to a testing distance of 25cm according to Radner et al. 1998.

2. Contrast sensitivity of the study eye. The contrast sensitivity is defined as the lowest contrast level, at which two of the three letters are read correctly. In examinations where the number of letters read correctly is 0 for the contrast level 0.00, the interpretation "no contrasts were recognized" was applied.

3.and 4. Eye specific quality of life and *Stability of fixation.* The German version of the National Eye Institute Visual Function Questionnaire (NEI-VFQ), which was adapted and validated by Franke et al. (1998), was used. The UK site used the original NEI-VFQ tests (English version). The evaluation of the eye specific quality of life was performed for the 12 sub-scales and for the composite score of the NEI-VFQ questionnaire (Mangione (2000)). The English version of the NEI-VFQ includes one more question than the German version: Question 16 A, which assesses the difficulties to drive under difficult conditions, was not asked in the German version. To make comparable the German and the English version, this question is excluded from the analysis.

5. Absolute number of letters read correctly in the study eye. The absolute number of letters read correctly on the ETDRS charts is evaluated as a further secondary endpoint.

2.6 Statistical Methods

The statistical analyses were performed using SAS 9.1. The analysis of the primary endpoint has to be interpreted as confirmative. All other analyses are regarded as explorative (hypothesis generating). Both graphical methods (box-whiskers plots) and analytical methods (calculation of the mean, median, first and third quartile, minimum, maximum, standard deviation; absolute and relative frequencies) are used for performing descriptive statistics.

2.6.1 Analysis of the Primary Endpoint

The analysis of the primary endpoint is based on the intention to treat principle (ITT). The primary endpoint was evaluated for the full analysis set (part 4.1). The Mann-Whitney-U test was used because of the non-normality of the data.

The statistical hypotheses are the following:

H_0: $F_{MT} \equiv F_{ST}$ and

H_1: $F_{MT} \not\equiv F_{ST}$,

where F_{MT} is the distribution function of the difference in the visual acuity in the study eye in the MT group, F_{ST} is the distribution function of the difference in the visual acuity in the study eye the ST group. Much fewer patients than the planned sample size were recruited. The interim analysis provided in the study protocol was rendered unnecessary. Therefore, a significance level of $\alpha = 0.05$ for the analysis of the primary endpoint is used.

2.6.2 Analysis of the Secondary Endpoints

All secondary endpoints (see part 2.5) were evaluated using the Mann-Whitney-U test. Each test was performed at a significance level of $\alpha = 0.05$. An adjustment for multiple testing was not done. The results of all tests are regarded as hypothesis-generating.

2.6.3 Safety Analysis

All adverse events are presented in table form. The proportion (incl. 95% confidence interval) of patients with at least one SAE is calculated for ST group and for MT group according to Wilson (1927). Furthermore, the difference of proportions (incl. 95% confidence interval) of patients with at least one SAE is calculated (Newcombe 1998).

2.6.4 Further Analysis

The time course of the visual acuity in both groups is investigated using a linear mixed effects regression model.

2.6.5 Sample Size Calculation

An estimation of the required number of patients is based on the pilot studies on macular translocation (Wolf et al. (1999)), the long-term results of the ophthalmologic centers in Aachen and Cologne (unpublished data, Aachen 19 patients, Cologne 39 patients with occult CNV) and on the results of the patients with occult CNV in the ST group in the radiation trial (Holz et al. (1999)). The observed standard deviation of change over one year in visual acuity in the ST group of the radiation trial was 3.8 lines on the ETDRS chart. In the pilot study on macular rotation, the standard deviation was higher (6.1 lines). However, in the data accumulated in Aachen and Cologne, the standard deviation was 4.6 and 4.5 lines, respectively. For the sample size calculation, the variation under study conditions (observed in Heidelberg in the radiation trial) was assumed as a standard deviation of 4 lines. A mean difference in change of visual acuity over one year of 1.5 lines on the ETDRS chart was judged as clinically relevant.

An interim analysis was planned with the first half of the patients completing the one-year follow-up in order to enable an early stopping due to success or total failure of the new treatment. A sequential testing procedure according to O'Brien and Fleming (1979) should be used to adopt the significance level resulting in $\alpha_{interim} = 0.005$ and $\alpha_{final} = 0.048$ for the interim and the final analysis, respectively.

For a global significance level $\alpha = 0.05$ and with consideration of the interim analysis, a power of 90% requires 155 patients per group, i.e. a total of 310 patients for the whole trial.

2.6.6 Changes in the Study Protocol

The start of the MARAN trial was planned for 01/2003, the end was expected for 2005.

The study protocol was amended four times during the accomplishment of the trial. The dates for the amendments were:

Amendment 1: 10th of February, 2002

Amendment 2: 12th of July, 2002

Amendment 3: 11th of October, 2002

Amendment 4: 1st of October, 2003

For the justification and other details of the amendments, see the appendix.

2.6.7 Deviations of the Study Protocol

At the last study meeting in 2004, the stop of the MARAN trial was decided. Because of low recruiting, this trial was stopped after the randomization of 28 patients. A continuation of MARAN trial was ethically not justifiable. Thus, the interim analysis became unnecessary. Therefore, a significance level of $\alpha = 0.05$ was used for the final analysis.

In deviation from the study protocol, no variables to assess the stability of fixation were documented on the CRF. Thus, no analysis of this secondary endpoint could be performed.

3 Accomplishment of the Trial

3.1 Patients

In the time period between October 7, 2002 and June 14, 2004, 28 patients were randomized. Because of the low recruitment, the trial was stopped on July 1, 2004 (21 months after starting recruiting). All patients were enrolled in the two trial sites Cologne and Liverpool. All other sites were not initiated. For the trial site Liverpool, only the amendments 1 and 2 were applicable: For the amendments 3 and 4, the approval from the local ethics committee was granted only after randomization of the last patient. Thus, for all patients enrolled in Liverpool, the inclusion and exclusion criteria from the study protocol from August 17, 2001, were applied. For the patients recruited in Cologne, the regulations from Amendment 3 were applied for 11 patients (Patid = 9, 11, 12, 13, 15, 16, 17, 19, 20, 22, 23), the regulations from amendment 4 were applied for three patients (Patid = 25, 26, 27). Table 2 shows the patients recruitment in the trial sites and the result of the randomization.

Table 2: Patients recruitment in the trial sites and result of randomization.

Site	N=28	%
Cologne	15 (MT: 6, ST: 9)	53.6 (MT: 21.4, ST: 32.1)
Liverpool	13 (MT: 7, ST: 6)	46.4 (MT: 25.0, ST: 21.4)

An overview of the patients recruitment over time is shown in Figure 2.

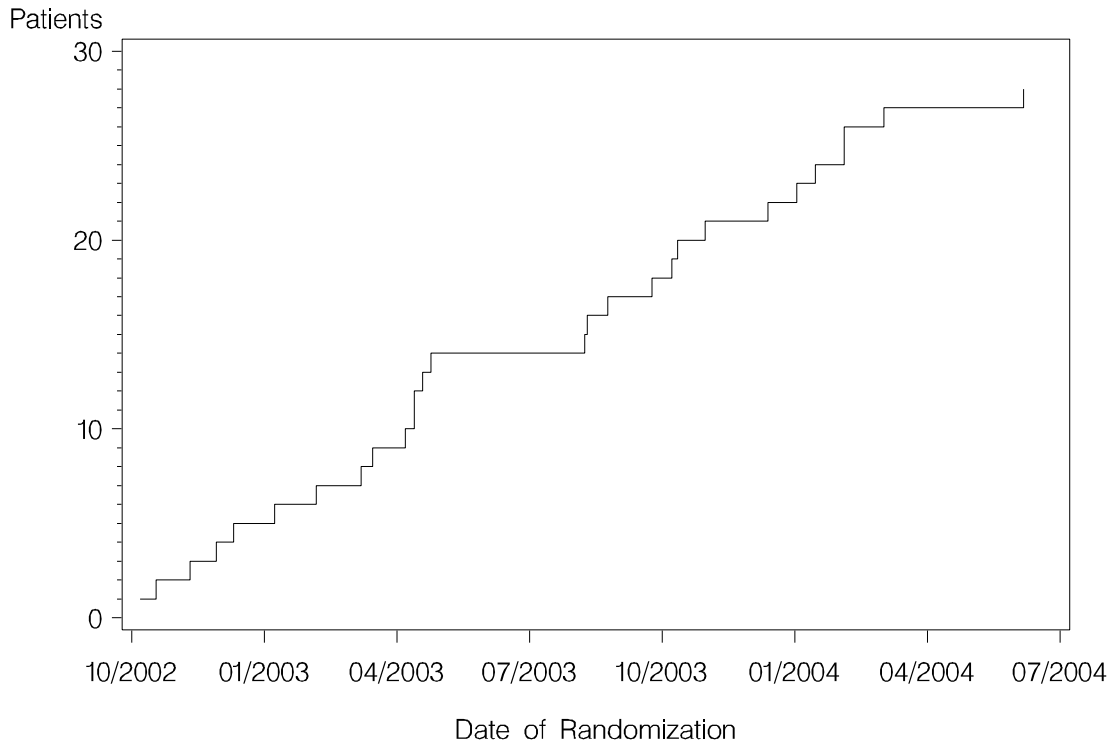

Figure 2: Patients recruitment over time.

The result of the randomization was an assignment of 13 patients to the MT group and of 15 patients to the ST group. One of the patients recruited in Cologne (Patid = 25) withdraw the study immediately after the randomization. This patient was randomized to the ST group and did not wish to continue the study because she preferred to be operated. Another patient recruited in Cologne withdraw the study after the control examination after 38 weeks (Patid = 22, randomized to the MT group). This patient was not able to come because of a very bad general condition. In one patient randomized to the ST group, macular translocation was performed about 6 weeks after randomization because this patient wanted macular translocation surgery (Patid = 11). In three patients randomized to the MT group, no macular translocation surgery was performed (Patid = 12, 15, 22). The reason was in all three cases a withdrawal of the consent for surgery after randomization to the MT group.

One patient randomized to the ST group died four weeks after the control examination in week 52 (Patid = 9, see part 5). The reason for this death is unknown. An overview of all patients in the MARAN trial shows the patients flow chart (see Figure 3).

The full analysis set (see 4.1) is identical to the ITT population, i.e. a strictly as-randomized analysis is performed for the primary endpoint.

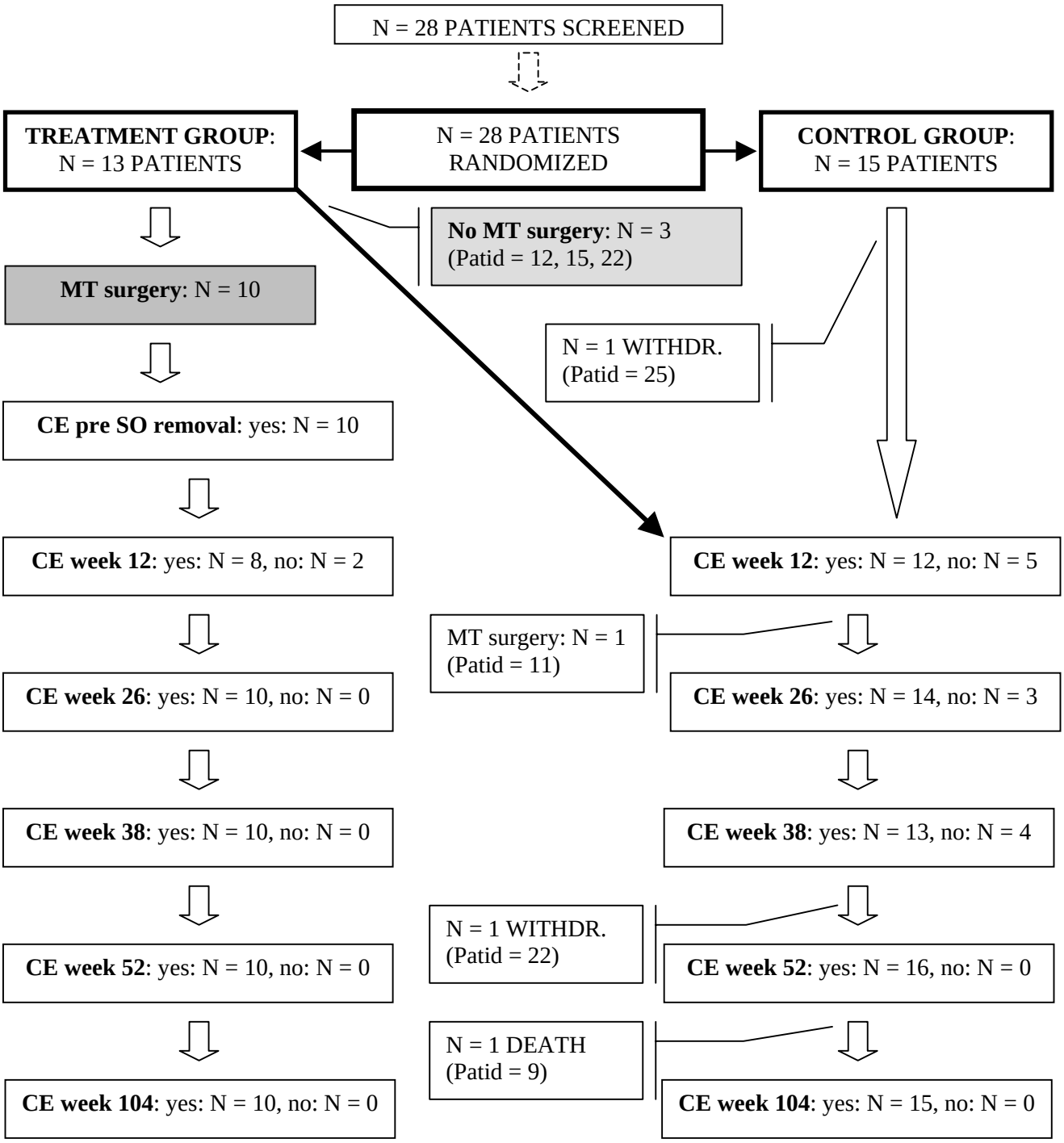

Figure 3: Patients Flow chart (CE: control examination, SO: silicone oil).

3.2 Protocol Violations, Data Quality

The time between the entry examination and the randomization should be between 0 and 14 days. This was exceeded in four patients randomized at the trial site Cologne (Patid = 15: 15 days, Patid = 16: 25 days, Patid = 19: 31 days, Patid = 23: 45 days). For all patients enrolled in the trial site Liverpool, the entry examination had been performed mistakenly before the randomization. In a 'note to file' it was stated that all patients randomized at the trial site Liverpool were eligible for the study participation. Furthermore, for all patients recruited in the trial site Liverpool, the reading performance was measured only from LogMAR 1.3 downwards, which was also confirmed in a 'note to file'.

In four patients randomized at the trial site Liverpool, the testing distance for measuring the visual acuity was at six occasions reduced from 4 meters to 2 meters. For the data analysis, these measurements were corrected using the number 10 instead of the number 20 in the numerator of the decimal equivalent of the visual acuity.

A total of 11 macular translocation surgeries were performed in the MARAN trial. Ten surgeries were performed in the MT group. In deviation from the study protocol, one surgery was performed in the ST group (Patid = 11), and in three patients randomized to the MT group, no surgery was performed (Patid = 12, 15, 22, see part see 3.1).

In summary, the following known major violations of the study protocol occurred during the accomplishment this trial:

- randomization before the entry examination,
- inclusion of patients violating the inclusion criteria,
- no performance of macular translocation surgery in patients randomized to the MT group,
- performance of macular translocation surgery in patients randomized to the ST group,
- incorrect testing distance.

Detailed information about known major protocol deviations are included in the appendix 11.1.

The quality of data cannot be assessed because only an incomplete clinical monitoring was performed in the MARAN trial (data source verification was performed only for trial site Cologne).

4 Results

4.1 Analysis Sets

The following analysis sets are used:

- *Full Analysis Set:* the full analysis set consists of all patients who were randomized. The full analysis set consists of 28 patients.
- *Safety Analysis Set:* The safety analysis set and the full analysis set are identical in the MARAN trial.

In the study protocol, no per-protocol-analysis was specified. Therefore, a *Per Protocol Set* will not be defined.

4.2 Baseline Characteristics

4.2.1 Demographic Characteristics

Table 3 shows the demographic characteristics at the entry examination for the whole study population and for both groups.

Table 3: Demographic characteristics (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Age [years]				
- N	13	15	28	0.9448 *[1]
- Mean +/- SD	71.9 +/- 6.1	71.8 +/- 7.0	71.9 +/-6.5	
- p5, p25, p75, p95	62.0, 66.0, 76.0, 82.0	58.0, 66.0, 78.0, 83.0	62.0, 66.0, 77.5, 82.0	
- Median	73.0	73.0	73.0	
- Min, Max	62.0, 82.0	58.0, 83.0	58.0, 83.0	
- 95% CI Mean	[68.2;75.6]	[67.9;75.7]	[69.3;74.4]	
- 95% CI Median	[66.0;78.0]	[66.0;78.0]	[67.0;76.0]	
Sex				
- male	2 (15.4%)	5 (33.3%)	7 (25.0%)	0.3955 *[3]
- female	11 (84.6%)	10 (66.7%)	21 (75.0%)	
Study Eye				
- right	5 (38.5%)	10 (66.7%)	15 (53.6%)	0.1356 *[2]
- left	8 (61.5%)	5 (33.3%)	13 (46.4%)	
Ethnic Group				
- Caucasian	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Smoking habits				
- non-smoker	1 (7.7%)	6 (40.0%)	7 (25.0%)	0.1353 *[3]
- current smoker	7 (53.8%)	4 (26.7%)	11 (39.3%)	
- ex-smoker	5 (38.5%)	5 (33.3%)	10 (35.7%)	
Iris color				
- blue	3 (23.1%)	11 (73.3%)	14 (50.0%)	0.0246 *[3]
- green	2 (15.4%)	1 (6.7%)	3 (10.7%)	
- brown	7 (53.8%)	3 (20.0%)	10 (35.7%)	
- other	1 (7.7%)	0 (0.0%)	1 (3.6%)	

*[1] = U-Test *[2] = chi^2 - Test *[3] = Fisher's Exact Test

The data show a difference between both groups in the iris color. A p-value of 0.02 is not unlikely in one of five tests. Because of the extern randomization by e-mail, the only explanation is that this difference is caused by chance. This difference will not be regarded as relevant for the primary and secondary endpoint.

4.2.2 Ophthalmological History of the Study Eye

The following tables summarizes the characteristics of the ophthalmological history of the study eye.

Table 4 shows the subfoveal choroidal neovascular membrane classification (fundus classification) for the study eye.

Table 4: Study eye: Fundus classification (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Fundus classification				
- occult	9 (69.2%)	13 (86.7%)	22 (78.6%)	0.3720 *[3]
- mixed (<50%classic)	4 (30.8%)	2 (13.3%)	6 (21.4%)	

*[3] = Fisher's Exact Test

Table 5 shows the results of the macula examination (RPE detachment, subretinal extrafoveal hemorrhage), and other examinations (dry eye syndrome, cataract, uveitis, glaucoma, ARMD, others).

Table 5: Study eye: Frequencies of RPE-detachment, subretinal extrafoveal hemorrhage, and other.

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
RPE-detachment				
- no	11 (84.6%)	12 (80.0%)	23 (82.1%)	1.0000*[3]
- yes	2 (15.4%)	3 (20.0%)	5 (17.9%)	
Subretinal extrafoveal hemorrhage				
- no	10 (76.9%)	10 (66.7%)	20 (71.4%)	0.6860 *[3]
- yes	3 (23.1%)	5 (33.3%)	8 (28.6%)	
Dry Eye Syndrome				
- no	11 (84.6%)	11 (73.3%)	22 (78.6%)	0.6546 *[3]
- yes	2 (15.4%)	4 (26.7%)	6 (21.4%)	
Cataract				
- no	8 (61.5%)	8 (53.3%)	16 (57.1%)	0.6617 *[2]
- yes	5 (38.5%)	7 (46.7%)	12 (42.9%)	
Uveitis				
- no	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Glaucoma				
- no	10 (76.9%)	14 (93.3%)	24 (85.7%)	0.3111 *[3]
- yes	3 (23.1%)	1 (6.7%)	4 (14.3%)	
ARMD				
- yes	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Other ophthalmologic anamnesis				
- no	7 (77.8%)	6 (75.0%)	13 (76.5%)	1.0000 *[3]
- yes	2 (22.2%)	2 (25.0%)	4 (23.5%)	
- missing	4	7	11	

*[2] = chi^2 - Test *[3] = Fisher's Exact Test

Other events in the ophthalmologic anamnesis of the study eye were recorded in four patients: RETROBULBAER INJECTION (Patid = 13), LIME BURN(KALKVERAETZUNG) (Patid = 15), CAT-OP RA (Patid = 22), CAT.-OP (Patid = 25).

The lens status and the status of dislocation of the study eye are summarized in Table 6.

Table 6: Study eye: Lens status and status of dislocation.

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Lens status				
- Phakia	10 (76.9%)	13 (86.7%)	23 (82.1%)	0.6389 *[3]
- Pseudophakia	3 (23.1%)	2 (13.3%)	5 (17.9%)	
Dislocation				
- no	12 (100.0%)	14 (100.0%)	26 (100.0%)	
- missing	1	1	2	

*[3] = Fisher's Exact Test

The results of further examinations of the study eye at the entry examination are included in appendix 11.2.1:

- Grading of cataract according LOCS III,
- Results of examination of differential light sensitivity in the visual field (Goldman perimetry),
- Results from slitlamp examination,
- Intraocular pressure (tonometry),
- Cyclorotation.

The data show that randomization produced comparable groups in the characteristics of ophthalmological history of the study eye.

4.2.3 Ophthalmological History of the Fellow Eye

Table 7 shows results of the examination of the fellow eye at the entry examination (dry eye syndrome, cataract, uveitis, glaucoma, ARMD, others).

Table 7: Fellow eye: Ophthalmological history.

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Dry Eye Syndrome				
- no	11 (84.6%)	11 (73.3%)	22 (78.6%)	0.6546 *[3]
- yes	2 (15.4%)	4 (26.7%)	6 (21.4%)	
Cataract				
- no	9 (69.2%)	8 (53.3%)	17 (60.7%)	0.3903 *[2]
- yes	4 (30.8%)	7 (46.7%)	11 (39.3%)	
Uveitis				
- no	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Glaucoma				
- no	10 (76.9%)	14 (93.3%)	24 (85.7%)	0.3111 *[3]
- yes	3 (23.1%)	1 (6.7%)	4 (14.3%)	
ARMD				
- no	0 (0.0%)	1 (6.7%)	1 (3.6%)	1.0000 *[3]
- yes	13 (100.0%)	14 (93.3%)	27 (96.4%)	
Other ophthalmologic amamnesis				
- no	7 (87.5%)	5 (62.5%)	12 (75.0%)	0.5692 *[3]
- yes	1 (12.5%)	3 (37.5%)	4 (25.0%)	
- missing	5	7	12	

*[2] = chi^2 - Test *[3] = Fisher's Exact Test

Other events in the ophthalmologic anamnesis of the fellow eye were recorded in four patients: PDT (3X) (Patid = 19), AMBLYOPIA (Patid = 22), CAT.-OP (Patid = 25), INJURY OPTIC ATROPHIE (Patid = 27). The lens status and the status of dislocation of the fellow eye is summarized in Table 8.

Table 8: Fellow eye: Lens status and status of dislocation.

	Treatment N=13	Control N=15	Total N=28	p-value
Lens status				
- Phakia	11 (84.6%)	13 (86.7%)	24 (85.7%)	1.0000 *[3]
- Pseudophakia	2 (15.4%)	2 (13.3%)	4 (14.3%)	
Dislocation				
- no	12 (100.0%)	14 (100.0%)	26 (100.0%)	
- missing	1	1	2	

*[3] = Fisher's Exact Test

The results of the grading of cataract according LOCS III and Cyclorotation of the fellow eye at the entry examination are included in the appendix 11.2.2. The data show that randomization produced comparable groups in the characteristics of the ophthalmological history of the fellow eye.

4.2.4 Ophthalmological History of the Patients

In this part, the ophthalmological history of the patients is described. Table 9 shows the duration time of losing reading ability, details of using visual aids, details of using devices, and the occurrence of eye diseases in family members. Table 10 shows the assessment of the binocular vision (Bagolini test and the Titmus test) at the entry examination.

Table 9: Ophthalmological history.

	Treatment N=13	Control N=15	Total N=28	p-value
Duration of loss of reading ability [weeks]				
- N	11	15	26	0.8113 *[1]
- Mean +/- SD	9.8 +/- 5.1	9.6 +/- 4.9	9.7 +/-4.9	
- p5, p25, p75, p95	0.0, 6.0, 14.0, 16.0	0.0, 8.0, 12.0, 20.0	0.0, 8.0, 12.0, 16.0	
- Median	12.0	8.0	8.0	
- Min, Max	0.0, 16.0	0.0, 20.0	0.0, 20.0	
- 95% CI Mean	[6.4;13.2]	[6.9;12.3]	[7.7;11.7]	
- 95% CI Median	[6.0;16.0]	[8.0;12.0]	[8.0;12.0]	
Visual Aids				
- Reading spectacles	2 (15.4%)	3 (20.0%)	5 (17.9%)	0.7971 *[3]
- Magnifying glasses	4 (30.8%)	7 (46.7%)	11 (39.3%)	
- TV or PC based magnification devices	1 (7.7%)	1 (6.7%)	2 (7.1%)	
- Read.spect.+magn.glasses	5 (38.5%)	3 (20.0%)	8 (28.6%)	
- Read.spect.+magn.glasses +TV/PC magn.	0 (0.0%)	1 (6.7%)	1 (3.6%)	
- Read.spect.+magn.glasses +Other	1 (7.7%)	0 (0.0%)	1 (3.6%)	
Eye diseases in family members				
- no	7 (53.8%)	9 (60.0%)	16 (57.1%)	0.7428 *[2]
- yes	6 (46.2%)	6 (40.0%)	12 (42.9%)	

*[1] = U-Test *[2] = chi^2 - Test *[3] = Fisher's Exact Test

Table 10: Binocular Vision (Entry Examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Baseline: Bagolini Test				
- Simultaneous	7 (53.8%)	9 (60.0%)	16 (57.1%)	0.6715 *[3]
- Exclusion right eye	4 (30.8%)	2 (13.3%)	6 (21.4%)	
- Exclusion left eye	2 (15.4%)	4 (26.7%)	6 (21.4%)	
Baseline: Titmus Test				
- Positive	5 (38.5%)	6 (40.0%)	11 (39.3%)	0.9337 *[2]
- Negative	8 (61.5%)	9 (60.0%)	17 (60.7%)	

*[2] = chi^2 - Test *[3] = Fisher's Exact Test

The data show that randomization produced comparable groups in the characteristics documented for the ophthalmological history and binocularity.

4.2.5 Medical History and Medications

Table 11 shows the frequencies of disorders documented in the CRF. Details of the diseases, diagnoses, hypersensitivities, and operations are included in the appendix 11.2.3.

Table 11: Frequencies of disorders.

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Cardiovascular system				
- normal	7 (53.8%)	5 (33.3%)	12 (42.9%)	0.2740 *[2]
- pathological	6 (46.2%)	10 (66.7%)	16 (57.1%)	
Hypertension				
- no	7 (53.8%)	10 (66.7%)	17 (60.7%)	0.4885 *[2]
- yes	6 (46.2%)	5 (33.3%)	11 (39.3%)	
Myocardial infarction				
- no	12 (92.3%)	12 (80.0%)	24 (85.7%)	0.6000 *[3]
- yes	1 (7.7%)	3 (20.0%)	4 (14.3%)	
Stroke				
- no	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Cardiovascular system: Others				
- no	12 (92.3%)	11 (73.3%)	23 (82.1%)	0.3333 *[3]
- yes	1 (7.7%)	4 (26.7%)	5 (17.9%)	
Gastrointestinal system				
- normal	11 (84.6%)	11 (73.3%)	22 (78.6%)	0.6546 *[3]
- pathological	2 (15.4%)	4 (26.7%)	6 (21.4%)	
Central nervous system				
- normal	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Bronchopulmonary system				
- normal	11 (84.6%)	12 (80.0%)	23 (82.1%)	1.0000 *[3]
- pathological	2 (15.4%)	3 (20.0%)	5 (17.9%)	
Endocrinology/Metabolism				
- normal	7 (53.8%)	9 (60.0%)	16 (57.1%)	0.7428 *[2]
- pathological	6 (46.2%)	6 (40.0%)	12 (42.9%)	
Hyperlipidemia				
- no	10 (76.9%)	12 (80.0%)	22 (78.6%)	1.0000 *[3]
- yes	3 (23.1%)	3 (20.0%)	6 (21.4%)	
Endocrinology/Metabolism: Others				
- no	8 (61.5%)	12 (80.0%)	20 (71.4%)	0.4097 *[3]
- yes	5 (38.5%)	3 (20.0%)	8 (28.6%)	
Medical History: Others				
- no	11 (84.6%)	9 (60.0%)	20 (71.4%)	0.2213 *[3]
- yes	2 (15.4%)	6 (40.0%)	8 (28.6%)	
Known Hypersensitivities				
- no	8 (61.5%)	13 (86.7%)	21 (75.0%)	0.1977 *[3]
- yes	5 (38.5%)	2 (13.3%)	7 (25.0%)	
Severe Operations				
- no	5 (38.5%)	6 (40.0%)	11 (39.3%)	0.9337 *[2]
- yes	8 (61.5%)	9 (60.0%)	17 (60.7%)	

*[2] = chi^2 - Test *[3] = Fisher's Exact Test

Furthermore, it was asked for the intake of acetylsalicylic acids, steroids, cumarine derivates, antihypertensive drugs, other systemic drugs, antiglaucomatous drugs, and other eye drugs. Table 12 shows

the frequencies of these medications. A listing of systemic drugs and other eye drugs is shown in the appendix 11.2.3.

Table 12: Frequencies of medications.

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Acetylsalicylic acid				
- no	8 (61.5%)	12 (80.0%)	20 (71.4%)	0.4097 *[3]
- yes	5 (38.5%)	3 (20.0%)	8 (28.6%)	
Steroids				
- no	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Cumarine derivates				
- no	12 (92.3%)	15 (100.0%)	27 (96.4%)	0.4643 *[3]
- yes	1 (7.7%)	0 (0.0%)	1 (3.6%)	
Antihypertensive drugs				
- no	7 (53.8%)	8 (53.3%)	15 (53.6%)	0.9784 *[2]
- yes	6 (46.2%)	7 (46.7%)	13 (46.4%)	
Other systemic drugs				
- no	2 (15.4%)	3 (20.0%)	5 (17.9%)	1.0000 *[3]
- yes	11 (84.6%)	12 (80.0%)	23 (82.1%)	
Antiglaucomatous drugs				
- no	10 (76.9%)	14 (93.3%)	24 (85.7%)	0.3111 *[3]
- yes	3 (23.1%)	1 (6.7%)	4 (14.3%)	
Other eye drugs				
- no	11 (84.6%)	11 (73.3%)	22 (78.6%)	0.6546 *[3]
- yes	2 (15.4%)	4 (26.7%)	6 (21.4%)	

*[2] = chi^2 - Test *[3] = Fisher's Exact Test

There data in Table 11 and Table 12 show that randomization produced comparable groups.

4.2.6 Assessment of the Study Eye

Table 13 shows the visual acuity (logMAR), the contrast sensitivity, the total number of correctly read letters, the reading performance, and the refraction measured in the study eye at the entry examination.

Table 13: Study eye: visual acuity (logMAR), contrast sensitivity, total number of correctly read letters, reading performance, refraction (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Visual acuity (ETDRS) - logMAR				
- N	13	15	28	0.8134 *[1]
- Mean +/- SD	0.7 +/- 0.2	0.7 +/- 0.2	0.7 +/-0.2	
- p5, p25, p75, p95	0.4, 0.5, 0.8, 1.2	0.5, 0.5, 0.8, 0.9	0.5, 0.5, 0.8, 1.0	
- Median	0.6	0.6	0.6	
- Min, Max	0.4, 1.2	0.5, 0.9	0.4, 1.2	
- 95% CI Median	[0.5;0.9]	[0.5;0.8]	[0.5;0.8]	
Contrast sensitivity				
- N	13	15	28	0.6391 *[1]
- Mean +/- SD	1.0 +/- 0.3	1.1 +/- 0.3	1.1 +/-0.3	
- p5, p25, p75, p95	0.5, 0.8, 1.2, 1.4	0.3, 0.9, 1.4, 1.7	0.5, 0.9, 1.3, 1.5	
- Median	1.2	1.2	1.2	
- Min, Max	0.5, 1.4	0.3, 1.7	0.3, 1.7	
- 95% CI Mean	[0.9;1.2]	[0.9;1.3]	[1.0;1.2]	
- 95% CI Median	[0.8;1.4]	[0.9;1.4]	[1.1;1.2]	
Total number of correctly read letters				
- N	13	15	28	0.8716 *[1]
- Mean +/- SD	50.4 +/- 12.9	51.6 +/- 8.4	51.0 +/-10.5	
- p5, p25, p75, p95	20.0, 43.0, 60.0, 64.0	35.0, 44.0, 58.0, 62.0	35.0, 43.5, 59.0, 62.0	
- Median	54.0	54.0	54.0	
- Min, Max	20.0, 64.0	35.0, 62.0	20.0, 64.0	
- 95% CI Median	[38.0;61.0]	[44.0;58.0]	[46.0;58.0]	
Reading performance				
- N	10	14	24	0.2272 *[1]
- Mean +/- SD	0.8 +/- 0.3	1.0 +/- 0.3	0.9 +/-0.3	
- p5, p25, p75, p95	0.5, 0.6, 0.9, 1.3	0.6, 0.7, 1.2, 1.5	0.6, 0.7, 1.2, 1.3	
- Median	0.8	0.9	0.9	
- Min, Max	0.5, 1.3	0.6, 1.5	0.5, 1.5	
- 95% CI Median	[0.6;1.2]	[0.7;1.3]	[0.7;1.1]	
Refraction - Sphere				
- N	13	15	28	0.0144 *[1]
- Mean +/- SD	0.1 +/- 1.6	1.9 +/- 1.8	1.1 +/-1.9	
- p5, p25, p75, p95	-4.0, -0.3, 1.0, 2.0	0.0, 0.5, 3.0, 7.0	-1.5, 0.1, 1.9, 3.8	
- Median	0.5	1.5	1.0	
- Min, Max	-4.0, 2.0	0.0, 7.0	-4.0, 7.0	
- 95% CI Median	[-1.0;1.0]	[0.5;3.0]	[0.3;1.8]	
Refraction - Cylinder				
- N	13	15	28	0.7749 *[1]
- Mean +/- SD	0.2 +/- 1.2	-0.0 +/- 0.7	0.1 +/-1.0	
- p5, p25, p75, p95	-1.0, -0.8, 0.5, 3.0	-1.5, -0.5, 0.5, 1.5	-1.0, -0.6, 0.5, 2.0	
- Median	0.0	0.0	0.0	
- Min, Max	-1.0, 3.0	-1.5, 1.5	-1.5, 3.0	
- 95% CI Median	[-1.0;0.8]	[-0.5;0.5]	[0.0;0.5]	
Refraction - Axis				
- N	13	15	28	0.4462 *[1]
- Mean +/- SD	87.3 +/- 66.4	66.7 +/- 71.6	76.3 +/-68.8	
- p5, p25, p75, p95	0.0, 0.0, 130.0, 175.0	0.0, 0.0, 100.0, 180.0	0.0, 0.0, 130.0, 180.0	
- Median	100.0	75.0	95.0	
- Min, Max	0.0, 175.0	0.0, 180.0	0.0, 180.0	
- 95% CI Median	[0.0;160.0]	[0.0;100.0]	[0.0;105.0]	

*[1] = U-Test

The data show a difference between both groups in the assessment of the sphere. In all other characteristics, the data show that randomization produced comparable groups.

4.2.7 Assessment of the Fellow Eye

In this part, the characteristics of the fellow eye measured at the entry examination are described. Table 14 shows the visual acuity, the total number of correctly read letters, and the refraction.

Table 14: Fellow eye: Visual acuity (logMAR), total number of correctly read letters, refraction (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Visual acuity (ETDRS) - logMAR				
- N	13	15	28	0.6599 *[1]
- Mean +/- SD	1.1 +/- 0.5	1.2 +/- 0.6	1.2 +/-0.6	
- p5, p25, p75, p95	0.0, 0.9, 1.5, 2.0	0.0, 1.0, 1.5, 2.1	0.0, 1.0, 1.5, 2.0	
- Median	1.3	1.4	1.3	
- Min, Max	0.0, 2.0	0.0, 2.1	0.0, 2.1	
- 95% CI Median	[0.8;1.5]	[1.0;1.5]	[1.0;1.4]	
Visual acuity (ETDRS) - decimal				
- N	13	15	28	0.3423 *[1]
- Mean +/- SD	0.1 +/- 0.1	0.0 +/- 0.0	0.1 +/-0.1	
- p5, p25, p75, p95	0.0, 0.0, 0.1, 0.3	0.0, 0.0, 0.1, 0.1	0.0, 0.0, 0.1, 0.2	
- Median	0.1	0.0	0.0	
- Min, Max	0.0, 0.3	0.0, 0.1	0.0, 0.3	
- 95% CI Median	[0.0;0.1]	[0.0;0.1]	[0.0;0.1]	
Total number of correctly read letters				
- N	13	15	28	0.4465 *[1]
- Mean +/- SD	22.7 +/- 18.5	16.3 +/- 13.7	19.3 +/-16.1	
- p5, p25, p75, p95	2.0, 10.0, 40.0, 63.0	0.0, 1.0, 25.0, 41.0	0.0, 4.0, 31.0, 41.0	
- Median	16.0	17.0	16.5	
- Min, Max	2.0, 63.0	0.0, 41.0	0.0, 63.0	
- 95% CI Median	[5.0;40.0]	[1.0;25.0]	[10.0;25.0]	
Refraction - Sphere				
- N	13	14	27	0.0171 *[1]
- Mean +/- SD	-0.0 +/- 1.2	1.6 +/- 2.1	0.8 +/-1.9	
- p5, p25, p75, p95	-2.3, -0.3, 0.5, 2.0	-1.3, 1.0, 3.0, 7.0	-2.0, -0.3, 1.5, 3.5	
- Median	0.0	1.3	0.8	
- Min, Max	-2.3, 2.0	-1.3, 7.0	-2.3, 7.0	
- 95% CI Median	[-1.0;0.8]	[1.0;3.5]	[0.0;1.3]	
Refraction - Cylinder				
- N	13	14	27	0.1996 *[1]
- Mean +/- SD	0.4 +/- 0.8	0.1 +/- 1.0	0.2 +/-0.9	
- p5, p25, p75, p95	-0.8, 0.0, 0.5, 2.0	-1.5, -0.5, 0.0, 2.8	-1.0, 0.0, 0.5, 2.0	
- Median	0.3	0.0	0.0	
- Min, Max	-0.8, 2.0	-1.5, 2.8	-1.5, 2.8	
- 95% CI Median	[0.0;1.5]	[-0.5;0.8]	[0.0;0.5]	
Refraction – Axis				
- N	13	14	27	0.6152 *[1]
- Mean +/- SD	58.5 +/- 58.6	50.0 +/- 60.5	54.1 +/-58.6	
- p5, p25, p75, p95	0.0, 0.0, 95.0, 180.0	0.0, 0.0, 95.0, 170.0	0.0, 0.0, 95.0, 170.0	
- Median	50.0	10.0	40.0	
- Min, Max	0.0, 180.0	0.0, 170.0	0.0, 180.0	
- 95% CI Median	[0.0;105.0]	[0.0;110.0]	[0.0;95.0]	

*[1] = U-Test

There is a difference between both groups in the assessment of the sphere. In all other characteristics, the data show that randomization produced comparable groups.

4.2.8 Eye specific Quality of Life

In this part, the evaluation of the eye specific quality of life at the entry examination is described. The description of the composite score is shown in Table 15.

Table 15: Composite score of the Visual Functioning Questionnaire (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Composite Score				
- N	13	15	28	0.5647 *[1]
- Mean +/- SD	54.5 +/- 17.4	50.9 +/- 12.4	52.6 +/-14.8	
- p5, p25, p75, p95	25.9, 41.2, 70.3, 80.2	25.9, 41.7, 57.0, 75.3	25.9, 41.4, 62.2, 75.3	
- Median	54.8	51.1	52.0	
- Min, Max	25.9, 80.2	25.9, 75.3	25.9, 80.2	
- 95% CI Median	[34.9;71.9]	[41.7;57.0]	[43.5;58.4]	

*[1] = U-Test

The description of the 12 sub-scales of the NEI VFQ is included in Table A 13 in the appendix 11.2.4. The data show that randomization produced comparable groups in the characteristics of eye specific quality of life.

The data presented in part 4.2 show that randomization produced comparable treatment groups in the demographic characteristics and in the other characteristics measured at baseline.

4.3 Characteristics measured at the Control Examinations

4.3.1 Anamnestic characteristics

Details of the following anamnestic characteristics measured at the control examinations in week 12, 26, 38, 52 and 104 are presented in the appendix 11.4: fundus classification for the study eye, RPE-detachment, subretinal extrafoveal hemorrhage in the study eye, grading of cataract according to the LOCS III (study eye and fellow eye), results of the examination of differential light sensitivity in the visual field of the study eye (Goldman perimetry), results from the slitlamp examination of the study eye, results from measuring the intraocular pressure in the study eye (tonometry), results from cyclorotation and binocularity.

4.3.2 Assessment of the Study Eye and the Fellow Eye

Figure 4 shows the time course of visual acuity in the study eye (logMAR) for both groups. The primary endpoint is the change of visual acuity (ETDRS) in week 52 after randomization compared to entry visual acuity (results: see part 6).

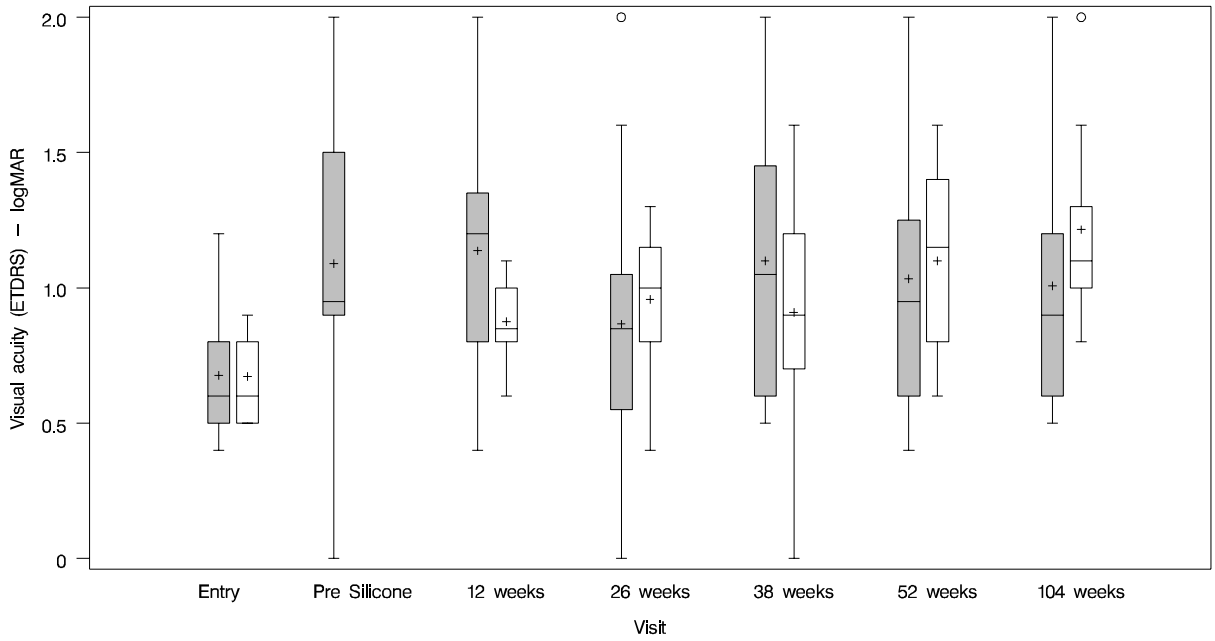

Figure 4: Time course of the visual acuity in the study eye for both groups (= MT group, = ST group). Greater values in the logMAR signify an impairment in visual acuity (see trial protocol, page 47).

Figure 4 shows an impairment of the visual acuity in the study eye after the macular translocation surgery was performed (MT group: entry examination versus examination pre silicone oil removal). The data show a better median visual acuity in the MT group at the control examinations in week 52 and week 104.
Figure 5 shows the time course of the visual acuity in the fellow eye (logMAR) for both groups.

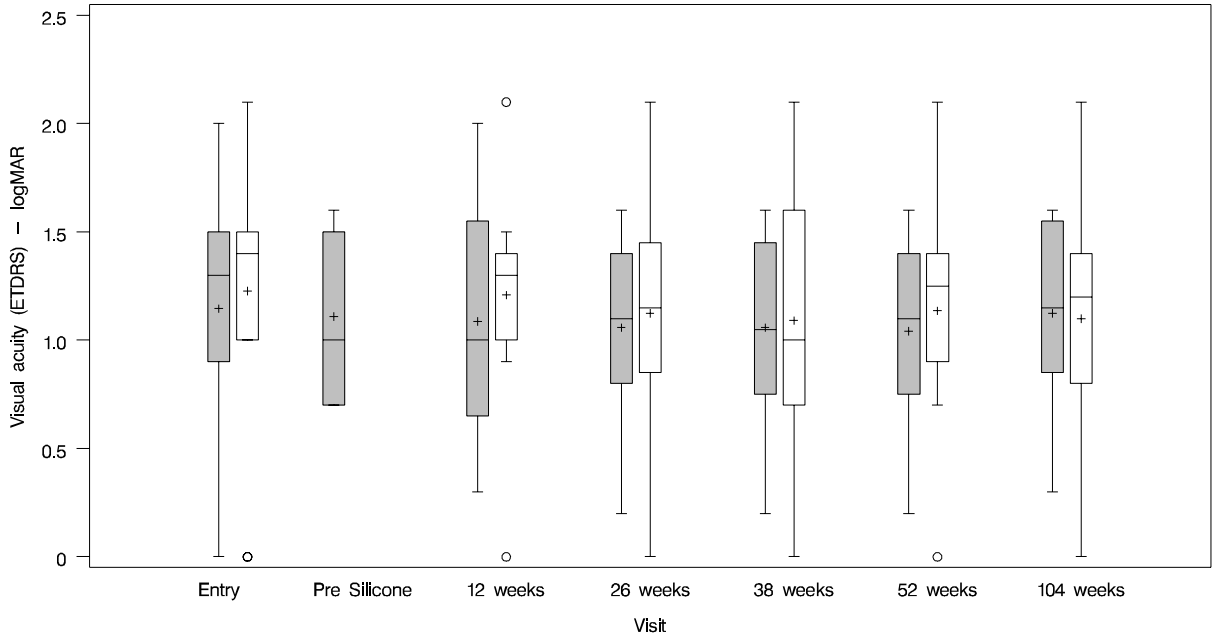

Figure 5: Time course of the visual acuity in the fellow eye for both groups (= MT group, = ST group). Greater values in the logMAR signify an impairment in visual acuity (see trial protocol, page 47).

Figure 5 shows that there are no obvious changes over time: Both in the MT group and in the ST group the visual acuity in the fellow eye seems to be constant over time.
The description of the refraction in the study eye and in the fellow eye at the control examinations in week 12, 26, 38, 52 and 104 is presented in the appendix 11.4 (Table A 26 and Table A 27).

4.3.3 Eye specific Quality of Life

Details of the assessment of the eye specific quality of life are shown in the appendix 11.5.

4.4 Performance of Treatment

4.4.1 Macular Translocation Surgery

Thirteen patients were randomized to the MT group. In three of these patients, no macular translocation surgery was performed (Patid = 12, 15, 22, see 3.1). The reason was that all three patients withdrew consent for the surgery after being randomized to the MT group.
Macular translocation surgery was performed in 10 patients randomized to the MT group. In one patient (Patid = 23), the detachment was achieved by a combination of the transvitreal approach and the transscleral approach. In this patient the macular translocation was downward. In all other patients the detachment was achieved by a transvitreal approach and the macular translocation was upward. There were anaesthesia problems in two patients. Intraoperative complications were observed in three patients. Further details of surgery performance are summarized in Table A 14 in the appendix 11.3.
Muscular counterrotation was nowhere performed during the macular translocation surgery, but in 9 of the 10 patients muscular counterrotation surgery was performed later (see 4.4.3).
In one patient randomized to the ST group (Patid = 11, see 3.1), the macular translocation was performed about 6 weeks after randomization, because this patient wished the performance of macular translocation surgery. For this patient, no detailed information about surgery is available. Muscular counterrotation surgery in this patient was performed 13 weeks later.

4.4.2 Characteristics measured at the Control Examination pre silicone oil removal

For those 10 patients (MT group) in which the macular translocation surgery was performed, information of AE's and life threatening conditions at the time-point control examination pre silicone oil removal is available. Table 16 shows frequencies of AE's and SAE's for this time-point. In all other AE's and SAE's asked on the CRF, no events were reported.

Table 16: AE's (study eye) and SAE's at the time point control examination pre silicone oil removal.

	Operated Patients N=10
Study Eye: Infection of the eye	
- no	9 (90.0%)
- moderate	1 (10.0%)
Study Eye: Pheripheral visual field defects	
- no	9 (90.0%)
- moderate	1 (10.0%)
Study Eye: Dry Eye Syndrome	
- no	9 (90.0%)
- moderate	1 (10.0%)
Study Eye: Perception of tilted images	
- no	4 (40.0%)
- mild	3 (30.0%)
- moderate	1 (10.0%)
- severe	2 (20.0%)
Study Eye: IOP > 22 mmHg	
- no	8 (80.0%)
- mild	1 (10.0%)
- moderate	1 (10.0%)
Study Eye: Other AE	
- no	8 (80.0%)
- mild	1 (10.0%)
- moderate	1 (10.0%)
Any other unscheduled hospitalization	
- no	8 (80.0%)
- yes	2 (20.0%)

There were two serious adverse events reported in the study eye (any other unscheduled hospitalization):

- Patid = 6: CARDIAC ARRHYTHMIAS NOTICED DURING ANAESTHETIC - PATIENT TRANSFERRED TO CARDIAC WARD POST OP FOR MONITORING OVERNIGHT. AWAITING REVIEW AND PROBABLE DISCHARGE BY CARDIOLOGIST
- Patid = 23: INPATIENT HOSPITALIZATION BY PRESUMPTION DIAGNOSIS: SERIOUS PANCREATITS.

For the fellow eye, no adverse events were reported at the time point control examination "pre silicone oil removal". No life threatening conditions were observed in any patient.

4.4.3 Muscular Counterrotation Surgery

Muscular counterrotation surgery was performed in 9 patients randomized to the MT group who underwent macular translocation surgery. Furthermore, muscular counterrotation surgery was performed in a patient who underwent macular translocation surgery in spite of randomization to the ST group (see 4.4.1). Details of the performance of the muscular counterrotation surgery are summarized in Table A 16 in the appendix.

All documented macular translocation surgeries were performed as upward translocation. For Patid = 23, no information about the muscular counterrotation surgery is available.

4.4.4 Eye specific interventions

In total, eye specific interventions were documented in three patients randomized to the ST group and in 9 patients randomized to the MT group. Table 17 summarizes these interventions.

Table 17: Eye specific interventions.

Patient Identification	Examin.	Intervention
001/11/female/66/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
		Study Eye: Cataract surgery
002/11/male/83/Control	104 weeks	Fellow Eye: Cataract surgery
003/01/female/65/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
		Study Eye: Cataract surgery
	52 weeks	Study Eye: Silicone oil removal
004/11/female/75/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
		Study Eye: Cataract surgery
006/11/female/79/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
009/01/female/76/Control	52 weeks	Study Eye: Cataract surgery
		Study Eye: Photodynamic Therapy (PDT)
010/11/male/73/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
011/01/female/69/Control	52 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
		Study Eye: Cataract surgery
		Study Eye: Secondary cataract
014/11/female/76/Translocation	26 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
017/01/female/71/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
	26 weeks	Study Eye: Cataract surgery
018/11/female/66/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation
028/11/female/68/Translocation	12 weeks	Study Eye: Silicone oil removal
		Study Eye: Muscular Counterrotation

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

5 Evaluation of Safety

At each control examination

- eye-specific AE's were asked for the study eye and for the fellow eye: infection of the eye, macular pucker, optic atrophy, peripheral visual field defects, dry eye syndrome, uveitis, perception of tilted images, other eye-specific adverse events; furthermore: late macular edema, persistent postoperative elevated intraocular pressure (IOP>22 mm Hg) and retinal traction detachment (PVR) for the study eye,
- AE's observed in the patient were documented (headache, any newly diagnosed systemic disease, other).

Additionally, the severity (mild, moderate, severe) of each event was reported.

SAE's were reported using the following three categories:

- eye-specific SAE's of the study eye and eye-specific SAE's of the fellow eye: endophthalmitis, loss of eye, complete loss of vision,
- SAE's observed in the patient: In-patient hospitalization in case of fractures, unscheduled operation of the study eye, any other unscheduled hospitalization, death,
- life threatening conditions: cardiovascular system (myocardial infarction, stroke, others), central nervous system, endocrinologic system, gastrointestinal system, bronchopulmonary system, urogenital system, others.

Table 18 shows the frequencies of patients with at least one reported AE and the severity of the AE, for the study eye and for the fellow eye.

Table 18: Frequencies of patients with at least one AE and severity of AE's (study eye and fellow eye).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Study Eye: Infection of the eye				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Fellow Eye: Infection of the eye				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Macular pucker				
- no	12 (92.3%)	14 (100.0%)	26 (96.3%)	0.4815 *[3]
- mild	1 (7.7%)	0 (0.0%)	1 (3.7%)	
Fellow Eye: Macular pucker				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Optic Atrophy				
- no	12 (92.3%)	14 (100.0%)	26 (96.3%)	0.4815 *[3]
- moderate	1 (7.7%)	0 (0.0%)	1 (3.7%)	
Fellow Eye: Optic Atrophy				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Pheripheral visual field defects				
- no	11 (84.6%)	14 (100.0%)	25 (92.6%)	0.2222 *[3]
- moderate	2 (15.4%)	0 (0.0%)	2 (7.4%)	
Fellow Eye: Pheripheral visual field defects				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Dry Eye Syndrome				
- no	9 (69.2%)	9 (64.3%)	18 (66.7%)	0.7237 *[3]
- mild	2 (15.4%)	4 (28.6%)	6 (22.2%)	
- moderate	2 (15.4%)	1 (7.1%)	3 (11.1%)	
Fellow Eye: Dry Eye Syndrome				
- no	11 (84.6%)	9 (64.3%)	20 (74.1%)	0.5562 *[3]
- mild	1 (7.7%)	4 (28.6%)	5 (18.5%)	
- moderate	1 (7.7%)	1 (7.1%)	2 (7.4%)	
Study Eye: Uveitis				
- no	12 (92.3%)	14 (100.0%)	26 (96.3%)	0.4815 *[3]
- mild	1 (7.7%)	0 (0.0%)	1 (3.7%)	
Fellow Eye: Uveitis				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Perception of tilted images				
- no	5 (38.5%)	14 (100.0%)	19 (70.4%)	<0.001*[3]
- mild	1 (7.7%)	0 (0.0%)	1 (3.7%)	
- moderate	3 (23.1%)	0 (0.0%)	3 (11.1%)	
- severe	4 (30.8%)	0 (0.0%)	4 (14.8%)	
Fellow Eye: Perception of tilted images				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Late macular edema				
- no	10 (76.9%)	12 (85.7%)	22 (81.5%)	0.6835 *[3]
- mild	2 (15.4%)	1 (7.1%)	3 (11.1%)	
- moderate	1 (7.7%)	0 (0.0%)	1 (3.7%)	
- severe	0 (0.0%)	1 (7.1%)	1 (3.7%)	

	Treatment N=13	Control N=15	Total N=28	p-value
Study Eye: IOP > 22 mmHg				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Retinal traction detachment (PVR)				
- no	11 (84.6%)	14 (100.0%)	25 (92.6%)	0.2222 *[3]
- moderate	2 (15.4%)	0 (0.0%)	2 (7.4%)	
Study Eye: Others				
- no	8 (61.5%)	13 (92.9%)	21 (77.8%)	0.0768 *[3]
- yes	5 (38.5%)	1 (7.1%)	6 (22.2%)	
Fellow Eye: Others				
- no	13 (100.0%)	13 (92.9%)	26 (96.3%)	1.0000 *[3]
- yes	0 (0.0%)	1 (7.1%)	1 (3.7%)	

*[3] = Fisher's Exact Test

The data show an occurrence of perception of tilted images only in the MT group, being an effect of the macular translocation surgery. There were no effects in only five patients randomized to the MT group (Patid = 12, 15, 18, 22 and 28). In three of these patients, no macular translocation surgery was performed (Patid = 12, 15, 22, see part 3.1).

In all other AE's, the data show no indication of any difference between both groups.

Table 19 shows the frequencies of patients with at least one reported SAE and/or life threatening condition.

Table 19: Frequencies of patients with SAE's and/or life threatening condition.

	Treatment N=13	Control N=15	Total N=28	p-value
Study Eye: Endophthalmitis				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Fellow Eye: Endophthalmitis				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Loss of eye				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Fellow Eye: Loss of eye				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Study Eye: Loss of vision				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Fellow Eye: Loss of vision				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
In-patient hospitalization in case of fracture				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Unscheduled operation of the study eye				
- no	12 (92.3%)	14 (100.0%)	26 (96.3%)	0.4815 *[3]
- yes	1 (7.7%)	0 (0.0%)	1 (3.7%)	
Any other unscheduled hospitalization				
- no	10 (76.9%)	11 (78.6%)	21 (77.8%)	1.0000 *[3]
- yes	3 (23.1%)	3 (21.4%)	6 (22.2%)	
Death				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Myocardial infarction				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Stroke				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Cardiovascular system: Other AE				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Central nervous system				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Endocrinologic system				
- no	13 (100.0%)	14 (100.0%)	27 (100.0%)	
Gastrointestinal system				
- no	13 (100.0%)	13 (92.9%)	26 (96.3%)	1.0000 *[3]
- yes	0 (0.0%)	1 (7.1%)	1 (3.7%)	
Bronchopulmonary system				
- no	13 (100.0%)	13 (92.9%)	26 (96.3%)	1.0000 *[3]
- yes	0 (0.0%)	1 (7.1%)	1 (3.7%)	
Urogenital system				
- no	13 (100.0%)	13 (92.9%)	26 (96.3%)	1.0000 *[3]
- yes	0 (0.0%)	1 (7.1%)	1 (3.7%)	

	Treatment N=13	Control N=15	Total N=28	p-value
Other life threatening condition				
- no	13 (100.0%)	13 (92.9%)	26 (96.3%)	1.0000 *[3]
- yes	0 (0.0%)	1 (7.1%)	1 (3.7%)	

*[3] = Fisher's Exact Test

In total, SAE's were reported in 11 patients (MT group: n = 4, ST group: n = 7). One female patient randomized to the ST group (Patid = 9) died about 52 weeks after randomization. The reason for her death is unknown, a relation to the study intervention is unassessable/unclassifiable. She was randomized at an age of 76 years. Because of the mean age of the trial population (see Table 3), deaths are not unlikely to occur. In the other six SAE's reported in the patients randomized to the ST group, a relation to the study intervention was also unlikely (Patid = 2, 5, 7, 13, 19, 24). The proportion of patients with at least one SAE is in ST group 0.47 (95% CI: [0.248; 0.699]).

In one patient randomized to MT group (Patid = 3), two SAE's with certain relation to the study intervention were reported (two unscheduled operations of study eye). In the other three patients randomized to the MT group, a relation between the SAE's and study intervention was unlikely (Patid = 6, 17, 23). The proportion of patients with at least one SAE is in MT group 0.31 (95% CI: [0.127; 0.576]).

The data do not show a difference between the MT group and the ST group in the proportion of patients with at least one SAE (p=0.39, chi^2 Test, 95% confidence interval for the difference of the proportions: -0.16; 95% CI [-0.453; 0.187]).

Details of all 12 SAE's are listed in the following Table 20.

Table 20: Listing of SAE's.

Patient Identification	Start	End	ong?	Symptom/Diagnosis	Description	Outcome	Relation
002/11/male/83/Control	04/02/2004	13/02/2004		Other life threatening condition	SEPTICAEMIA (E COLI) FOLLOWING KNEE REPLACEMENT SURGERY	Recovered with sequelae	Unlikely
003/01/female/65/Translocation	12/02/2003		yes	Unscheduled operation of the study eye	NETZHAUTABLOESUNG DURCH PVR, OP HEUTE: RE-PPV, LC, OEL 5000	Ongoing at time of report	Certain
003/01/female/65/Translocation	28/08/2003	28/08/2003		Unscheduled operation of the study eye	INTRAOPERATIVE MEMBRAN PEELING AND GAS-TAMPONADE NECESSARY	Recovered with sequelae	Certain
005/11/female/77/Control	27/10/2003	31/10/2003		Gastrointestinal system	ADMITTED TO HOSPITAL WITH CHEST PAIN, INFLAMMATORY OESOPHAGUS TREATED WITH ZOTON IS NOW BETTER.	Recovered with sequelae	Unlikely
006/11/female/79/Translocation	30/01/2003		yes	Cardiovascular system: Others	CARDIAC ARRHYTHMIAS NOTICED DURING ANAESTHETIC - PATIENT TRANSFERRED TO CARDIAC WARD POST OP FOR MONITORING OVERNIGHT. AWAITING REVIEW AND PROBABLE DISCHARGE BY CARDIOLOGIST	Ongoing at time of report	Unlikely
007/11/female/73/Control	19/01/2004	15/02/2004		Bronchopulmonary system	EPISODE G BRONCHITIS LEADING TO PNEUMONIA. NO HOSPITAL ADMISSION, TREATED WITH ANTIBIOTICS AND STEROIDS (CONTROL PATIENT)	Recovered with sequelae	Unlikely
009/01/female/76/Control	NK/NK/2004	NK/NK/2004		Death	REASON OF DEATH IS UNKNOWN	Death	Unassessible/unclassifiable
013/01/female/79/Control	19/01/2004	09/02/2004		Any other unscheduled hospitalization	DIVERTICULITIS SIGMA-COLON-RESECTION	Recovered with sequelae	Unlikely
017/01/female/71/Translocation	NK/01/2005	NK/01/2005		Any other unscheduled hospitalization	1 WEEK HOSPITALIZATION BY INCOMPATIBILITY OF ANTIBIOTICO. THESE WERE TAKEN AS POSTOPERATIVE TREATMENT AFTER SURGERY (AMBULANT) 9/04 OF A RELAPSE OF THE BENIGN TUMOR AT THE LEFT CERVIX (MED. HISTORY).	Recovered with sequelae	Unlikely
019/01/female/69/Control	30/11/2004	12/12/2004		Any other unscheduled hospitalization Gastrointestinal system	DIVERTICOLOSIS WITH RESECTION OF COLON	Recovered with sequelae	Unlikely
023/01/female/78/Translocation	09/02/2004	09/04/2004		Any other unscheduled hospitalization	INPATIENT HOSPITALIZATION BY PRESUMPTION DIAGNOSIS: SERIOUS PANCREATITS	Recovered with sequelae	Unlikely
024/11/female/78/Control	NK/04/2004		yes	Urogenital system	PATIENT INFORMED US HAS HAD STRESS INCONTINENCE FOR LAST 18 MONTHS. (TODAY 16/01/2006)	Ongoing at time of report	Unlikely

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

6 Confirmatory Data Analysis

In this part the analysis of the primary endpoint is described. The primary endpoint (i.e. the change of the visual acuity (ETDRS) in the study eye, measured at 52 weeks after randomization compared to the visual acuity at the entry examination) is expressed in logMAR. The analysis of the primary endpoint is based on the intention-to-treat principle. Because of the non-normality of the difference in the visual acuity, the Mann-Whitney U-test is performed to investigate differences between both groups. In total, the primary endpoint is available from 26 patients: From two patients (Patid = 22 randomized to the MT group, Patid = 25 randomized to the ST group), only measurements from the entry examination are available (see part 3.1). A calculation of the primary endpoint was not possible for these two patients, and a strategy for the replacement of missing values in the primary endpoint was not specified in the study protocol. Therefore, the data from 26 patients were used in the analysis of the primary endpoint. Additionally, a sensitivity analysis was performed to investigate the impact of these patients in the analysis of the primary endpoint (part 6.3).

6.1 Analysis of the Primary Endpoint

Table 21 shows the descriptive statistics of the primary endpoint in each group. Positive differences mean an impairment of visual acuity, negative differences mean an improvement of visual acuity. For details of definition of the logMAR values, see page 47 of the study protocol.

Table 21: Primary endpoint: difference in the visual acuity (logMAR) in the study eye.

	Treatment N=13	**Control N=15**	**Total N=28**
Difference in the visual acuity (logMAR)			
- N	12	14	26
- Mean +/- SD	0.4 +/- 0.5	0.4 +/- 0.4	0.4 +/-0.5
- p5, p25, p75, p95	-0.4, -0.1, 0.7, 1.5	-0.2, 0.1, 0.7, 1.1	-0.2, -0.1, 0.7, 1.1
- Median	0.4	0.5	0.5
- Min, Max	-0.4, 1.5	-0.2, 1.1	-0.4, 1.5
- 95% CI Median	[-0.1;0.7]	[0.1;0.8]	[0.1;0.6]

Positive differences: impairment in visual acuity; negative differences: improvement in visual acuity.

The confirmatory data analysis shows no significant difference between both groups: p=0.80, Mann-Whitney-U-test. According to Altman et al. (2000), the median difference between both groups is estimated as -0.05 logMAR, and the confidence interval for the difference of the medians between the MT group and the ST group is from -0.5 logMAR to 0.3 logMAR. A negative difference between MT group and ST group (i.e. the greater change in visual acuity in the ST group), implies an advantage for the MT group (i.e. the smaller change). A positive difference between MT group and ST group (i.e. the greater change in visual acuity in the MT group), implies an advantage for the ST group (i.e. the smaller change in the ST group).
There is a positive median change of the visual acuity in each group (0.4 logMAR in the MT group, 0.5 logMAR in the ST group), showing an impairment of the visual acuity from randomization to the control examination in week 52 (see also Figure 4).

6.2 Effects of the Trial Sites

Table 22 shows the descriptive statistics of the primary endpoint for each trial site.

Table 22: Primary endpoint: difference in the visual acuity (logMAR) in the study eye for each trial site.

	Treatment N=13	**Control N=15**	**Total N=28**
Difference in the visual acuity (logMAR) in Site Cologne			
- N	5	8	13
- Mean +/- SD	0.5 +/- 0.6	0.3 +/- 0.5	0.4 +/-0.5
- p5, p25, p75, p95	-0.1, 0.1, 0.7, 1.5	-0.2, -0.1, 0.6, 1.1	-0.2, -0.1, 0.7, 1.5
- Median	0.5	0.1	0.1
- Min, Max	-0.1, 1.5	-0.2, 1.1	-0.2, 1.5
- 95% CI Median	[-0.1;1.5]	[-0.1;1.1]	[-0.1;0.8]
Difference in the visual acuity (logMAR) in Site Liverpool			
- N	7	6	13
- Mean +/- SD	0.2 +/- 0.4	0.6 +/- 0.2	0.4 +/-0.4
- p5, p25, p75, p95	-0.4, -0.1, 0.6, 0.8	0.4, 0.5, 0.7, 1.0	-0.4, 0.2, 0.6, 1.0
- Median	0.2	0.6	0.5
- Min, Max	-0.4, 0.8	0.4, 1.0	-0.4, 1.0
- 95% CI Median	[-0.4;0.8]	[0.4;1.0]	[-0.1;0.7]

For each trial site, there is no difference between both groups (Mann-Whitney-U-test for the trial site Cologne: p=0.44, Mann-Whitney-U-test for the trial site Liverpool: p=0.22). There is a median impairment of the visual acuity observed in both groups in each trial site.

Regarding the median change of the visual acuity, there are opposite effects in both trial sites. In the trial site Cologne, the median impairment in the MT group was greater (0.5 logMAR), whereas in the trial site Liverpool, the median impairment in the ST group was greater (0.6 logMAR).

There could be various possibilities for the explanation of such an effect of trial site, but a conclusion could not be made because of the small sample sizes.

6.3 Sensitivity Analysis

In this part, results of a sensitivity analysis regarding the primary endpoint are presented. The primary endpoint is not available for two patients (Patid = 22, randomized to the MT group and Patid = 25, randomized to the ST group, see part 3.1). Both patients were recruited in the trial site Cologne. For these patients, the missing values in the visual acuity at the control examination in week 52 after randomization were replaced, following a ‘worst case scenario’ for the MT group and a ‘best case scenario’ for the MT group. In the former situation, the maximal observed impairment in the MT group was assumed for patient 22 (i.e. a change of 1.5 logMAR); the maximal observed improvement in the ST group was assumed for patient 25 (i.e. a change of -0.2 logMAR). In the latter situation, the maximal observed improvement in the MT group was assumed for patient 22 (i.e. a change of -0.4 logMAR); the maximal observed impairment in the ST group was assumed for patient 25 (i.e. a change of 1.1 logMAR). For the explorative analysis of both scenarios, the Mann-Whitney- U-test was performed. In both scenarios, there was no difference between the

groups (‘worst case scenario’: p=0.77 and ‘best case scenario’: p=0.43). These results support the result from the confirmatory analysis of the primary endpoint in part 6.1.

7 Analysis of the Secondary Endpoints

In this part, the results from the analysis of the secondary endpoints are presented. The differences (measured at 52 weeks after randomization and at the entry examination) in the following criteria were specified as secondary endpoints: Reading performance of the study eye, contrast sensitivity of the study eye, eye specific quality of life, absolute number of correctly read letters for the study eye. For a more detailed definition, see part 2.5 and part 2.6.

All results of the analysis of the secondary endpoints are regarded as explorative and not as proof of efficacy of the treatment.

7.1 Reading Performance of the Study Eye

Table 23 shows the change in the reading performance of the study eye (difference in the logMAR values for a testing distance of 25cm).

Table 23: Secondary endpoints: difference in reading performance (logMAR) of the study eye.

	Treatment N=13	**Control N=15**	**Total N=28**
Difference in the reading performance			
- N	12	14	26
- Mean +/- SD	0.1 +/- 0.9	0.5 +/- 0.5	0.3 +/-0.7
- p5, p25, p75, p95	-1.3, -0.5, 0.7, 1.4	0.0, 0.1, 1.1, 1.4	-1.2, 0.0, 0.8, 1.4
- Median	0.2	0.3	0.3
- Min, Max	-1.3, 1.4	0.0, 1.4	-1.3, 1.4
- 95% CI Median	[-0.7;0.7]	[0.1;1.1]	[0.0;0.7]

The data show no indication of any difference between both groups in the difference in reading performance (p=0.25, Mann-Whitney-U-test).

Figure 6 shows the time course of the reading performance (logMAR) in the study eye for both groups.

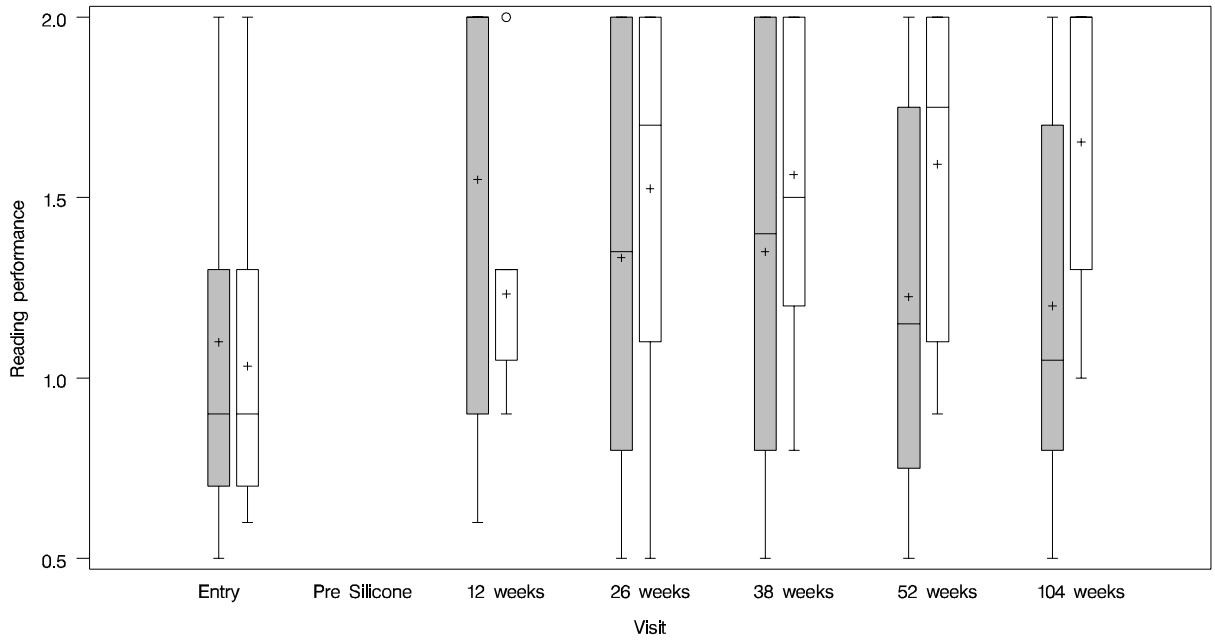

Figure 6: Time course of the reading performance (logMAR) in the study eye (= MT group, = ST group).

7.2 Contrast Sensitivity of the Study Eye

Table 24 shows the change in the contrast sensitivity of the study eye.

Table 24: Secondary endpoints: difference in the contrast sensitivity of the study eye.

	Treatment N=13	**Control N=15**	**Total N=28**
Difference in the contrast sensitivity			
- N	10	14	24
- Mean +/- SD	-0.0 +/- 0.3	-0.3 +/- 0.6	-0.2 +/-0.5
- p5, p25, p75, p95	-0.6, -0.3, 0.3, 0.5	-1.5, -0.8, 0.2, 0.3	-1.1, -0.5, 0.2, 0.3
- Median	-0.1	0.0	0.0
- Min, Max	-0.6, 0.5	-1.5, 0.3	-1.5, 0.5
- 95% CI Median	[-0.5;0.3]	[-0.8;0.2]	[-0.3;0.2]

The data show no evidence for a difference between both groups in the change in the contrast sensitivity of the study eye (Mann-Whitney-U-test: p=0.37).

Figure 7 shows the time course of the contrast sensitivity in the study eye for both groups.

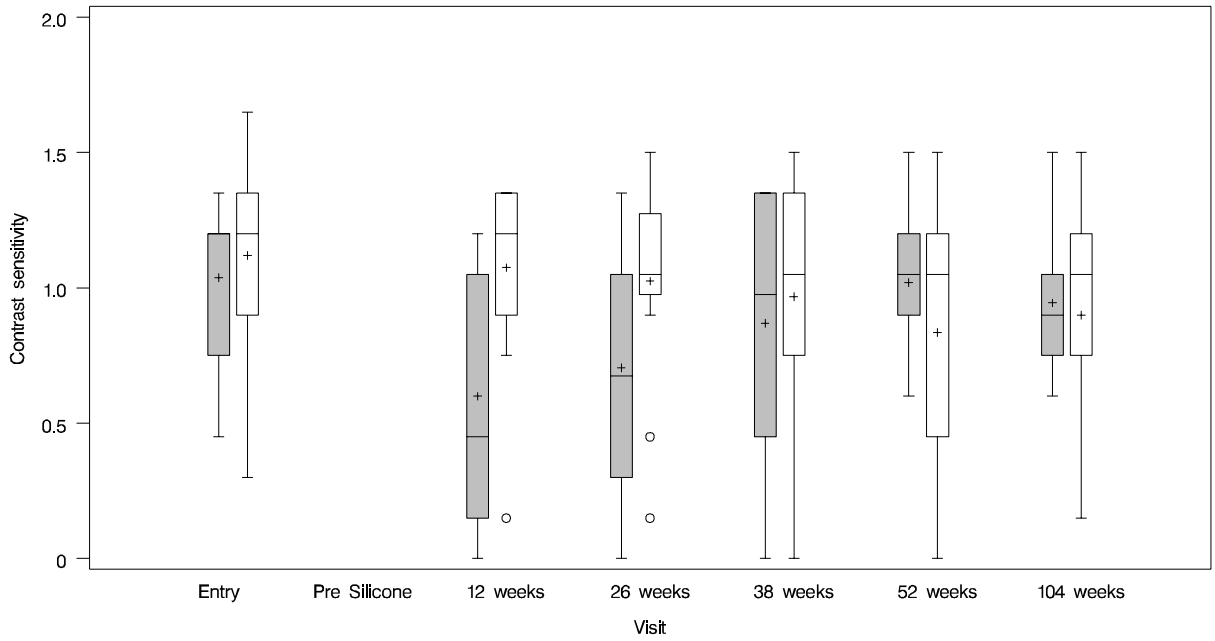

Figure 7: Time course of the contrast sensitivity in the study eye (= MT group, = ST group).

7.3 Eye specific quality of life

Table 25 shows the change in the 12 sub scales and the difference in the composite score of the NEI-VFQ questionnaire.

Table 25: Secondary endpoints: difference in the 12 sub scales and in the composite score of NEI-VFQ questionnaire.

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Difference: General Health				
- N	12	14	26	0.4914 *[1]
- Mean +/- SD	-8.3 +/- 12.3	-1.8 +/- 20.7	-4.8 +/-17.3	
- p5, p25, p75, p95	-25.0, -25.0, 0.0, 0.0	-25.0, -25.0, 0.0, 50.0	-25.0, -25.0, 0.0, 25.0	
- Median	0.0	0.0	0.0	
- Min, Max	-25.0, 0.0	-25.0, 50.0	-25.0, 50.0	
- 95% CI Median	[-25.0;0.0]	[-25.0;0.0]	[-25.0;0.0]	
Difference: General Vision				
- N	12	14	26	0.7137 *[1]
- Mean +/- SD	3.3 +/- 14.4	2.9 +/- 19.0	3.1 +/-16.7	
- p5, p25, p75, p95	-20.0, 0.0, 20.0, 20.0	-20.0, 0.0, 0.0, 40.0	-20.0, 0.0, 20.0, 40.0	
- Median	0.0	0.0	0.0	
- Min, Max	-20.0, 20.0	-20.0, 40.0	-20.0, 40.0	
- 95% CI Median	[0.0;20.0]	[0.0;20.0]	[0.0;0.0]	
Difference: Ocular Pain				
- N	12	14	26	0.9786 *[1]
- Mean +/- SD	3.1 +/- 27.8	-0.9 +/- 9.1	1.0 +/-19.7	
- p5, p25, p75, p95	-37.5, -12.5, 18.8, 62.5	-12.5, -12.5, 0.0, 12.5	-25.0, -12.5, 12.5, 37.5	
- Median	0.0	0.0	0.0	
- Min, Max	-37.5, 62.5	-12.5, 12.5	-37.5, 62.5	
- 95% CI Median	[-12.5;25.0]	[-12.5;12.5]	[-12.5;0.0]	
Difference: Near Activities				
- N	12	14	26	0.1529 *[1]
- Mean +/- SD	3.5 +/- 24.5	-7.7 +/- 10.6	-2.6 +/-18.8	
- p5, p25, p75, p95	-33.3, -20.8, 16.7, 50.0	-25.0, -16.7, 0.0, 8.3	-25.0, -16.7, 8.3, 25.0	
- Median	8.3	-4.2	0.0	
- Min, Max	-33.3, 50.0	-25.0, 8.3	-33.3, 50.0	
- 95% CI Median	[-25.0;16.7]	[-16.7;0.0]	[-16.7;8.3]	
Difference: Distance Activities				
- N	12	14	26	0.1710 *[1]
- Mean +/- SD	-9.4 +/- 22.1	-0.3 +/- 15.5	-4.5 +/-19.0	
- p5, p25, p75, p95	-41.7, -25.0, 8.3, 25.0	-33.3, -8.3, 8.3, 25.0	-33.3, -16.7, 8.3, 25.0	
- Median	-14.6	0.0	-4.2	
- Min, Max	-41.7, 25.0	-33.3, 25.0	-41.7, 25.0	
- 95% CI Median	[-25.0;16.7]	[-8.3;8.3]	[-16.7;8.3]	
Difference: Vision Specific: Social Functioning				
- N	12	14	26	0.3274 *[1]
- Mean +/- SD	-3.1 +/- 24.5	5.4 +/- 22.3	1.4 +/-23.3	
- p5, p25, p75, p95	-37.5, -25.0, 6.3, 50.0	-12.5, -12.5, 12.5, 75.0	-25.0, -12.5, 12.5, 50.0	
- Median	0.0	0.0	0.0	
- Min, Max	-37.5, 50.0	-12.5, 75.0	-37.5, 75.0	
- 95% CI Median	[-25.0;12.5]	[-12.5;12.5]	[-12.5;12.5]	
Difference: Vision Specific: Mental Health				
- N	12	14	26	0.4053 *[1]
- Mean +/- SD	4.2 +/- 22.0	7.1 +/- 16.8	5.8 +/-19.0	
- p5, p25, p75, p95	-43.8, -3.1, 9.4, 43.8	-31.3, 0.0, 18.8, 37.5	-31.3, 0.0, 12.5, 37.5	
- Median	0.0	6.3	6.3	
- Min, Max	-43.8, 43.8	-31.3, 37.5	-43.8, 43.8	
- 95% CI Median	[-6.3;12.5]	[0.0;18.8]	[0.0;12.5]	
Difference: Vision Specific: Role Difficulties				
- N	12	14	26	0.6580 *[1]
- Mean +/- SD	-8.3 +/- 33.9	-8.0 +/- 23.8	-8.2 +/-28.3	
- p5, p25, p75, p95	-62.5, -25.0, 6.3, 75.0	-50.0, -25.0, 12.5, 25.0	-50.0, -25.0, 12.5, 25.0	

	Treatment N=13	Control N=15	Total N=28	p-value
- Median	-12.5	-6.3	-12.5	
- Min, Max	-62.5, 75.0	-50.0, 25.0	-62.5, 75.0	
- 95% CI Median	[-25.0;12.5]	[-25.0;12.5]	[-25.0;0.0]	
Difference: Vision Specific: Dependency				
- N	12	14	26	0.5874 *[1]
- Mean +/- SD	-10.4 +/- 23.3	-19.6 +/- 31.5	-15.4 +/-27.9	
- p5, p25, p75, p95	-50.0, -29.2, 4.2, 25.0	-91.7, -41.7, 8.3, 16.7	-58.3, -33.3, 8.3, 16.7	
- Median	-4.2	-12.5	-8.3	
- Min, Max	-50.0, 25.0	-91.7, 16.7	-91.7, 25.0	
- 95% CI Median	[-33.3;8.3]	[-41.7;8.3]	[-33.3;0.0]	
Difference: Color Vision				
- N	12	14	26	0.2753 *[1]
- Mean +/- SD	-10.4 +/- 29.1	0.0 +/- 17.0	-4.8 +/-23.5	
- p5, p25, p75, p95	-50.0, -37.5, 0.0, 50.0	-25.0, 0.0, 0.0, 25.0	-50.0, -25.0, 0.0, 25.0	
- Median	0.0	0.0	0.0	
- Min, Max	-50.0, 50.0	-25.0, 25.0	-50.0, 50.0	
- 95% CI Median	[-50.0;0.0]	[0.0;25.0]	[0.0;0.0]	
Difference: Peripheral Vision				
- N	12	13	25	0.2626 *[1]
- Mean +/- SD	-20.8 +/- 31.7	-7.7 +/- 18.8	-14.0 +/-26.1	
- p5, p25, p75, p95	-75.0, -50.0, 0.0, 25.0	-50.0, -25.0, 0.0, 25.0	-50.0, -25.0, 0.0, 25.0	
- Median	-25.0	0.0	0.0	
- Min, Max	-75.0, 25.0	-50.0, 25.0	-75.0, 25.0	
- 95% CI Median	[-50.0;0.0]	[-25.0;0.0]	[-25.0;0.0]	
Difference: Composite Score				
- N	12	14	26	0.3961 *[1]
- Mean +/- SD	-4.7 +/- 13.2	-2.3 +/- 9.1	-3.4 +/-11.0	
- p5, p25, p75, p95	-21.0, -12.8, 1.2, 23.9	-19.0, -9.4, 4.2, 13.1	-19.0, -11.0, 4.2, 14.5	
- Median	-9.3	-0.5	-3.8	
- Min, Max	-21.0, 23.9	-19.0, 13.1	-21.0, 23.9	
- 95% CI Median	[-14.5;4.6]	[-9.4;4.6]	[-10.8;2.9]	

*[1] = U-Test

The data show no evidence for a difference between both groups, neither in the composite score nor in any sub-scale.

7.4 Absolute Number of Letters Read Correctly in the Study Eye

Table 26 shows the change in the number of letters read correctly in the study eye.

Table 26: Secondary endpoints: difference in the absolute numbers of letters read correctly in the study eye (week 52 minus baseline).

	Treatment N=13	Control N=15	Total N=28
Difference in the total number of correctly read letters			
- N	12	14	26
- Mean +/- SD	-12.6 +/- 22.2	-20.6 +/- 20.0	-16.9 +/-21.0
- p5, p25, p75, p95	-60.0, -25.5, 7.5, 17.0	-48.0, -38.0, -1.0, 10.0	-48.0, -31.0, -1.0, 10.0
- Median	-11.5	-20.0	-18.0
- Min, Max	-60.0, 17.0	-48.0, 10.0	-60.0, 17.0
- 95% CI Median	[-29.0;8.0]	[-38.0;-1.0]	[-31.0;-1.0]

The data show no evidence of a difference between both groups regarding the number of letters read correctly in the study eye (Mann-Whitney-U-test: p=0.34). The median changes show an impairment for both groups in the number of letters read correctly in the study eye.

Figure 8 shows the time course of the contrast sensitivity in the study eye for both groups.

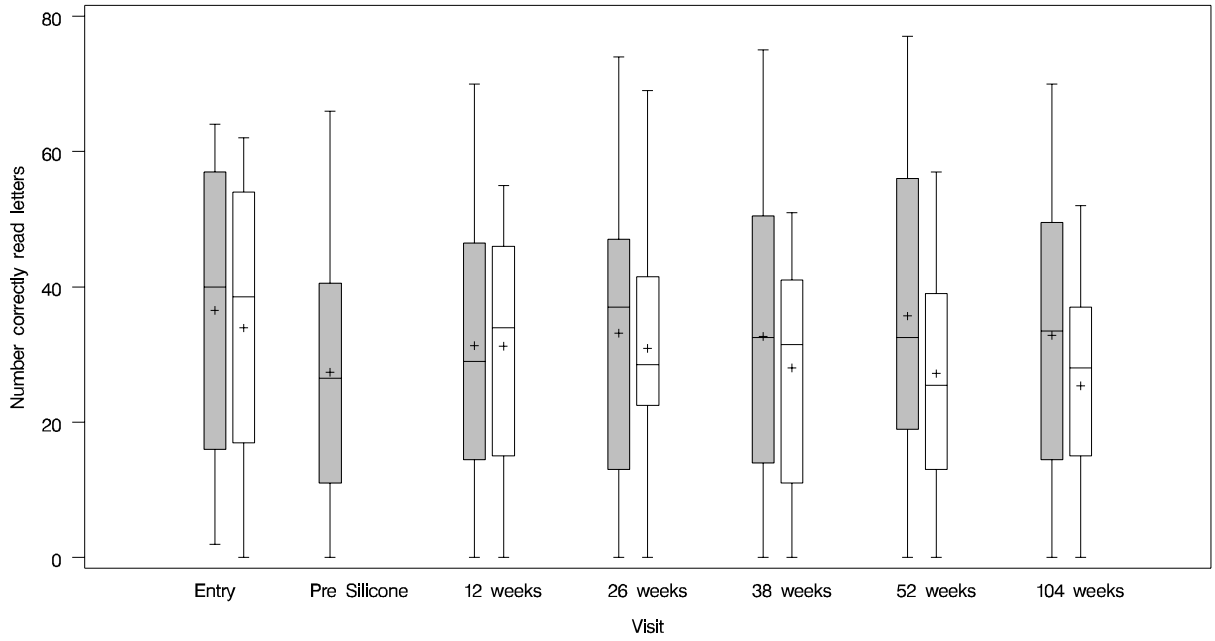

Figure 8: Time course of the number of correctly read letters in the study eye (= MT group, = ST group).

8 Further explorative Analysis

In this part, the results from further explorative data analyses are presented, namely:

- changes of visual acuity in the study eye, measured at week 104 after randomization compared to the visual acuity at the entry examination,
- changes of visual acuity in the fellow eye, measured at week 104 after randomization compared to the visual acuity at the entry examination,

results from the investigation of the time course of the visual acuity in the study eye (linear mixed effects regression analysis).

Table 27and Table 28 show the differences in the visual acuity (logMAR) of the study eye, respectively, the fellow eye, measured at week 104 after randomization compared to the visual acuity at the entry examination.

Table 27: Difference in the visual acuity (logMAR) of the study eye (week 104 minus baseline).

	Treatment N=13	**Control N=15**	**Total N=28**
Difference in the visual acuity			
- N	12	13	25
- Mean +/- SD	0.3 +/- 0.5	0.5 +/- 0.4	0.4 +/-0.5
- p5, p25, p75, p95	-0.4, -0.1, 0.6, 1.5	0.0, 0.2, 0.6, 1.5	-0.1, 0.1, 0.6, 1.5
- Median	0.3	0.6	0.4
- Min, Max	-0.4, 1.5	0.0, 1.5	-0.4, 1.5
- 95% CI Median	[-0.1;0.6]	[0.2;0.8]	[0.1;0.6]

Table 28: Difference in the visual acuity (logMAR) of the fellow eye (week 104 minus baseline).

	Treatment N=13	**Control N=15**	**Total N=28**
Difference in the visual acuity			
- N	12	13	25
- Mean +/- SD	0.0 +/- 0.6	-0.2 +/- 0.2	-0.1 +/-0.4
- p5, p25, p75, p95	-0.5, -0.3, 0.0, 1.6	-0.7, -0.3, 0.0, 0.3	-0.5, -0.3, 0.0, 0.3
- Median	-0.1	-0.2	-0.1
- Min, Max	-0.5, 1.6	-0.7, 0.3	-0.7, 1.6
- 95% CI Median	[-0.4;0.1]	[-0.3;0.0]	[-0.2;0.0]

The data show no difference between both groups (study eye, Mann-Whitney-U-test: p=0.20; fellow eye, Mann-Whitney-U-test: p=0.68).

To investigate the time course of the visual acuity in the study eye, a linear mixed effects regression model was fitted using proc mixed in SAS. The fixed effects were visual acuity at baseline, group, and time after randomization. The results show that there is no influence on the visual acuity in the three fixed effects investigated:

- visual acuity at baseline (WALD test: p=0.79)
- group (WALD test: p=0.76)
- time after randomization (WALD test: p=0.13)

Details of the model fit shows the appendix 11.6.

9 Summary and Conclusions

The MARAN trial aimed at evaluating the efficacy of a new surgical approach in ARMD and was designed as a multicenter, prospective, randomized (1:1) clinical trial with two study arms. The trial was planned to include 310 patients. Recruitment was slow, and in spite of extending the inclusion criteria, the recruitment could not be accelerated. Thus, the MARAN trial was stopped after the recruitment of only 28 patients, 21 months after randomizing the first patient. The reasons for this slow recruitment may be the fear of possible risks and side-effects of the surgical approach.

The randomization results in largely equality of structure between both arms (with exception of the refraction (sphere)). The validity of the study is limited: Many deviations from the trial protocol occurred, and only an incomplete monitoring was performed (data source verification only for trial site Cologne, no visits for the

trial site Liverpool). Furthermore, the number of patients is very low, and three patients randomized to the MT group violated the treatment recommendation and refused macular translocation surgery.

The confirmatory analysis shows no superiority of the macular translocation surgery in adult patients with clinical signs of exudative ARMD due to subfoveal choroidal neovascularization: The null-hypothesis of equality in the change in the visual acuity in the study eye could not be rejected. The sensitivity analysis and the analysis of the secondary endpoints confirm this result. A median impairment of the visual acuity was observed in both groups. Regarding the median change of the visual acuity, there were opposite effects in both trial sites (in Cologne, the greater median impairment was observed in the MT group; in Liverpool, the greater median impairment was observed in the ST group). An explanation of this effect of the trial site could not be made because of the small sample sizes.

The safety analysis has shown a difference in the perception of tilted images, which are an expected effect of the macular translocation surgery. In the other AE's and SAE's asked on the CRF, the data show no difference between both groups. In all patients who underwent macular translocation surgery, muscular counterrotation surgery had to be performed later.
One patient randomized to the ST group died during participation. The relation of death and study intervention was unassessable/unclassifiable, but seems unlikely, at least.

A superiority of macular translocation surgery could not be shown in the MARAN trial. In patients who underwent macular translocation surgery, additional therapeutic options had to be required (muscular counterrotation surgery, unscheduled operations of the study eye).

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11 Appendix

11.1 Known Protocol Violations

For all patients enrolled in the trial site Liverpool, the entry examination had been performed mistakenly before the randomization, see Table A 1.

Table A 1: Difference between randomization and entry examination (patients enrolled in Liverpool).

Patid	Siteid	Entry examination	Date of Randomization	Difference (days)
1	11	15/10/2002	07/10/2002	-8
2	11	29/10/2002	18/10/2002	-11
4	11	03/12/2002	29/11/2002	-4
5	11	17/12/2002	11/12/2002	-6
6	11	21/01/2003	09/01/2003	-12
7	11	18/02/2003	07/02/2003	-11
8	11	18/03/2003	10/03/2003	-8
10	11	22/04/2003	10/04/2003	-12
14	11	06/05/2003	28/04/2003	-8
18	11	24/02/2004	29/09/2003	-148
21	11	17/11/2003	05/11/2003	-12
24	11	02/02/2004	21/01/2004	-12
28	11	28/06/2004	14/06/2004	-14

The following listing summarizes other known major violations of the study protocol. The visual acuity is in the following expressed as decimal equivalent (see inclusion and exclusion criteria in part 2.3) and not in logMAR.

Patid = 1: In this patient, at the entry examination and at the examination pre silicone oil removal, the testing distance for the measurement of the visual acuity was 2 meters instead of 4 meters. The visual acuity in the study eye is 0.159 (not between 0.16 and 0.34, see the inclusion criteria). The visual acuity in the fellow eye is 0.313 (not 0.1 or less, see the inclusion criteria). The reason why the patient was randomized anyhow was reported as: “Patient was 20/100 in April 02 but 20/60 in September 02. The responsible physician said it was due to spontaneous improvement”.

Patid = 2: In this patient, at the entry examination and at the examination week 12 after randomization, the testing distance for the measurement of the visual acuity was 2 meters instead of 4 meters. The visual acuity in the study eye is 0.125 (not between 0.16 and 0.34, see the inclusion criteria). The duration of loss ability is 20 weeks (longer than 4 months, see the inclusion criteria). The reasons why the patient was randomized anyhow were reported as: “We think we got mixed up with decimal and logMAR.”, and “The responsible physician felt as this patient could still read with magnification he could still be randomized.”

Patid = 4: In this patient, at the entry examination, the testing distance for the measurement of the visual acuity was 2 meters instead of 4 meters. The visual acuity in the study eye is 0.125 (not between 0.16 and 0.34, see the inclusion criteria). The reason why the patient was randomized anyhow was reported as: “We may have confused decimal and logMAR”.

Patid = 5: In this patient, at the entry examination, the testing distance for the measurement of the visual acuity was 2 meters instead of 4 meters.

Patid = 6: In this patient, the inclusion criteria “Loss of reading ability (newsprint) no longer than 4 months (maximum optical addition for reading glasses is +3.0 dptr.)” is marked with “no”. The visual acuity in the study eye is 0.1 (not between 0.16 and 0.34, see the inclusion criteria). The reasons why the patient was randomized anyhow were reported as: “We got confused with logMAR and decimal”, and “As patient did not know, the responsible physician gave benefit on the doubt”. Furthermore, the duration of loss of reading ability is missing in this patient.

Patid = 10: In this patient, the visual acuity in the fellow eye is 0.125 (not 0.1 or less, see the inclusion criteria). The reason why the patient was randomized anyhow was reported as: “Known borderline. Confusion Decimal/logMAR. But fits criteria.”

Patid = 11: This patient was randomized to the ST group, but the macular translocation surgery was performed.

Patid = 12: This patient was randomized to the MT group, but the macular translocation surgery was not performed.

Patid = 14: In this patient, the visual acuity in the study eye is 0.0625 (not between 0.16 and 0.34, see the inclusion criteria). The visual acuity in the fellow eye is 0.16 (not 0.1 or less, see the inclusion criteria). The reasons why the patient was randomized anyhow were reported as: “Patient was randomized on 15.04.2003 when visus in FE was recorded as 3/60 = 20/317”, and “Unfortunately, her vision has dropped to below the inclusion criteria level since her entry examination on 25th March 2003. As she had agree to randomisation and was subsequently randomised to treatment, the responsible physician decided to go ahead with her surgery, which was carried out on 8th May 2003”.

Patid = 15: This patient was randomized to the MT group, but the macular translocation surgery was not performed.

Patid = 20: In this patient, the visual acuity in the study eye is 0.125 (not between 0.16 and 0.34, see the inclusion criteria). The reason why the patient was randomized anyhow was reported as: “Subject has been randomised by error”.

Patid = 22: This patient was randomized to the MT group, but the macular translocation surgery was not performed.

Patid = 24: In this patient, the visual acuity in the study eye is 0.125 (not between 0.16 and 0.34, see the inclusion criteria). The reason why the patient was randomized anyhow was reported as: “When recruited 15/12/2003 vision was logMAR 0.8. By entry examination 02/02/2004 vision had dropped.”

Patid = 27: The inclusion criteria “Evidence of ARMD in the fellow eye” is marked with “no”. The comment was “No sign of ARMD, blindness because of trauma.”

Patid = 28: In this patient, the visual acuity in the study eye is 0.40 (not between 0.16 and 0.34, see the inclusion criteria). The duration of loss of reading ability is missing. The reasons why the patient was randomized anyhow were given as: "When vision recorded 17/5/04 = logMAR 0.56 but improved on 28/06/04. After randomisation", and: "Patient was unsure, the responsible physician gave benefit of doubt".

11.2 Entry Examination: Further Results

11.2.1 Study Eye

In this part details of the further examinations of the study eye at the entry examination are presented.

Table A 2 shows the grading of cataract according to the Lens Opacities Classification System III (LOCS III). The LOCS III contains an expanded set of standards. It consists of six slit-lamp images for grading nuclear color (NC) and nuclear opalescence (NO), five retroillumination images for grading cortical cataract (C), and five retroillumination images for grading posterior subcapsular (P) cataract.

Table A 2: Study eye: Grading of cataract according to LOCS III (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Grading of cataract - NO				
- N	10	14	24	0.2352 *[1]
- Mean +/- SD	1.4 +/- 1.1	0.8 +/- 0.7	1.1 +/-0.9	
- p5, p25, p75, p95	0.2, 0.3, 2.0, 4.0	0.2, 0.2, 1.5, 2.0	0.2, 0.3, 1.8, 2.0	
- Median	1.5	0.4	1.0	
- Min, Max	0.2, 4.0	0.2, 2.0	0.2, 4.0	
- 95% CI Mean	[0.6;2.2]	[0.4;1.3]	[0.7;1.5]	
- 95% CI Median	[0.3;2.0]	[0.2;2.0]	[0.3;1.5]	
Grading of cataract - NC				
- N	10	14	24	0.2136 *[1]
- Mean +/- SD	1.5 +/- 1.2	0.9 +/- 0.8	1.2 +/-1.0	
- p5, p25, p75, p95	0.2, 0.3, 2.5, 4.0	0.2, 0.2, 2.0, 2.5	0.2, 0.3, 2.0, 2.5	
- Median	1.3	0.4	1.0	
- Min, Max	0.2, 4.0	0.2, 2.5	0.2, 4.0	
- 95% CI Mean	[0.7;2.4]	[0.4;1.4]	[0.7;1.6]	
- 95% CI Median	[0.3;2.5]	[0.2;2.0]	[0.3;2.0]	
Grading of cataract - C				
- N	10	14	24	0.7651 *[1]
- Mean +/- SD	0.7 +/- 1.1	0.8 +/- 1.0	0.8 +/-1.0	
- p5, p25, p75, p95	0.0, 0.1, 1.0, 3.5	0.1, 0.1, 1.0, 3.0	0.1, 0.1, 1.0, 3.0	
- Median	0.2	0.3	0.2	
- Min, Max	0.0, 3.5	0.1, 3.0	0.0, 3.5	
- 95% CI Mean	[-0.0;1.5]	[0.2;1.4]	[0.3;1.2]	
- 95% CI Median	[0.1;1.0]	[0.1;2.0]	[0.2;1.0]	
Grading of cataract - P				
- N	10	14	24	0.7002 *[1]
- Mean +/- SD	0.2 +/- 0.3	0.2 +/- 0.3	0.2 +/-0.3	
- p5, p25, p75, p95	0.0, 0.1, 0.2, 1.0	0.1, 0.1, 0.2, 1.0	0.1, 0.1, 0.2, 1.0	
- Median	0.1	0.1	0.1	
- Min, Max	0.0, 1.0	0.1, 1.0	0.0, 1.0	
- 95% CI Mean	[0.0;0.4]	[0.1;0.4]	[0.1;0.3]	
- 95% CI Median	[0.1;0.3]	[0.1;0.4]	[0.1;0.2]	

*[1] = U-Test

Table A 3 shows the results of the examination of differential light sensitivity in the visual field (Goldman perimetry). The visual field was recorded in the study eye using the standardized Goldmann apparatus. As test spot the III4 spot was used. Only the outer edges of the visual field were examined and added to the CRF. The outer edges of the visual field were documented along eight main meridians in degrees: superior (s), superior-nasal(sn), nasal (n), inferior-nasal (in), inferior (i), inferior-temporal (it), temporal (t), and temporal-superior (ts).

Table A 3: Study eye: Goldman Perimetry (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Goldman perimetry - Superior temporal margin				
- N	12	15	27	0.1066 *[1]
- Mean +/- SD	54.5 +/- 6.6	46.0 +/- 17.4	49.8 +/-14.1	
- p5, p25, p75, p95	43.0, 50.0, 58.5, 65.0	10.0, 35.0, 56.0, 75.0	20.0, 43.0, 58.0, 70.0	
- Median	56.0	48.0	55.0	
- Min, Max	43.0, 65.0	10.0, 75.0	10.0, 75.0	
- 95% CI Mean	[50.3;58.7]	[36.4;55.6]	[44.2;55.4]	
- 95% CI Median	[50.0;59.0]	[35.0;56.0]	[45.0;58.0]	
Goldman perimetry - Superior margin				
- N	12	15	27	0.2008 *[1]
- Mean +/- SD	42.9 +/- 6.3	37.9 +/- 10.2	40.1 +/-8.9	
- p5, p25, p75, p95	30.0, 40.0, 47.0, 52.0	20.0, 30.0, 48.0, 55.0	25.0, 32.0, 48.0, 52.0	
- Median	44.5	40.0	40.0	
- Min, Max	30.0, 52.0	20.0, 55.0	20.0, 55.0	
- 95% CI Mean	[38.9;46.9]	[32.3;43.6]	[36.6;43.7]	
- 95% CI Median	[40.0;48.0]	[30.0;48.0]	[35.0;46.0]	
Goldman perimetry - Superior nasal margin				
- N	12	15	27	0.2382 *[1]
- Mean +/- SD	48.4 +/- 6.6	43.3 +/- 12.9	45.6 +/-10.7	
- p5, p25, p75, p95	35.0, 44.5, 51.0, 58.0	18.0, 35.0, 55.0, 65.0	25.0, 38.0, 52.0, 60.0	
- Median	50.0	42.0	45.0	
- Min, Max	35.0, 58.0	18.0, 65.0	18.0, 65.0	
- 95% CI Mean	[44.3;52.6]	[36.1;50.4]	[41.3;49.8]	
- 95% CI Median	[44.0;52.0]	[35.0;55.0]	[40.0;50.0]	
Goldman perimetry - Temporal margin				
- N	12	15	27	0.2605 *[1]
- Mean +/- SD	66.2 +/- 10.0	60.3 +/- 15.7	62.9 +/-13.5	
- p5, p25, p75, p95	50.0, 57.5, 74.5, 81.0	22.0, 50.0, 70.0, 91.0	50.0, 53.0, 74.0, 81.0	
- Median	66.5	60.0	64.0	
- Min, Max	50.0, 81.0	22.0, 91.0	22.0, 91.0	
- 95% CI Mean	[59.8;72.5]	[51.7;69.0]	[57.6;68.3]	
- 95% CI Median	[57.0;75.0]	[50.0;70.0]	[57.0;72.0]	
Goldman perimetry - Nasal margin				
- N	12	15	27	1.0000 *[1]
- Mean +/- SD	50.0 +/- 9.2	51.1 +/- 11.2	50.6 +/-10.1	
- p5, p25, p75, p95	28.0, 45.5, 58.0, 60.0	30.0, 42.0, 60.0, 71.0	30.0, 45.0, 59.0, 68.0	
- Median	50.5	50.0	50.0	
- Min, Max	28.0, 60.0	30.0, 71.0	28.0, 71.0	
- 95% CI Mean	[44.2;55.8]	[44.9;57.3]	[46.6;54.6]	
- 95% CI Median	[45.0;58.0]	[42.0;60.0]	[46.0;58.0]	

	Treatment N=13	Control N=15	Total N=28	p-value
Goldman perimetry - Inferior temporal margin				
- N	12	15	27	0.4935 *[1]
- Mean +/- SD	64.8 +/- 14.3	62.9 +/- 16.6	63.8 +/-15.3	
- p5, p25, p75, p95	30.0, 57.5, 75.0, 80.0	15.0, 55.0, 70.0, 91.0	30.0, 55.0, 72.0, 80.0	
- Median	69.0	67.0	68.0	
- Min, Max	30.0, 80.0	15.0, 91.0	15.0, 91.0	
- 95% CI Mean	[55.7;73.9]	[53.8;72.1]	[57.7;69.8]	
- 95% CI Median	[55.0;76.0]	[55.0;70.0]	[62.0;70.0]	
Goldman perimetry - Inferior margin				
- N	12	15	27	0.3260 *[1]
- Mean +/- SD	55.9 +/- 12.9	53.3 +/- 13.8	54.5 +/-13.2	
- p5, p25, p75, p95	28.0, 48.5, 67.5, 69.0	15.0, 50.0, 60.0, 82.0	28.0, 50.0, 60.0, 69.0	
- Median	60.0	53.0	54.0	
- Min, Max	28.0, 69.0	15.0, 82.0	15.0, 82.0	
- 95% CI Mean	[47.7;64.1]	[45.7;61.0]	[49.3;59.7]	
- 95% CI Median	[44.0;68.0]	[50.0;60.0]	[52.0;60.0]	
Goldman perimetry - Inferior nasal margin				
- N	12	15	27	0.6940 *[1]
- Mean +/- SD	46.6 +/- 10.1	47.0 +/- 7.6	46.8 +/-8.6	
- p5, p25, p75, p95	20.0, 42.0, 52.5, 60.0	30.0, 45.0, 50.0, 66.0	30.0, 42.0, 50.0, 60.0	
- Median	48.0	46.0	47.0	
- Min, Max	20.0, 60.0	30.0, 66.0	20.0, 66.0	
- 95% CI Mean	[40.2;53.0]	[42.8;51.2]	[43.4;50.2]	
- 95% CI Median	[42.0;55.0]	[45.0;50.0]	[45.0;50.0]	

*[1] = U-Test

The results from the slitlamp examination shows Table A 4. The assessments of the anterior segment (external eye, cornea, anterior chamber, lens) and the assessment of the posterior segment (vitreous cavity, retinal attachment, retinal abnormalities, foveal position, recurrence) are presented.

Table A 4: Study eye: Slitlamp examination (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Slitlamp - External eye				
- Normal	11 (84.6%)	15 (100.0%)	26 (92.9%)	0.2063 *[3]
- Moderate inflammation	1 (7.7%)	0 (0.0%)	1 (3.6%)	
- Other	1 (7.7%)	0 (0.0%)	1 (3.6%)	
Slitlamp - Cornea				
- Normal	10 (76.9%)	14 (93.3%)	24 (85.7%)	0.4444 *[3]
- Dry Eye	1 (7.7%)	1 (6.7%)	2 (7.1%)	
- Other	2 (15.4%)	0 (0.0%)	2 (7.1%)	
Slitlamp - Anterior chamber				
- Normal	12 (100.0%)	14 (93.3%)	26 (96.3%)	1.0000 *[3]
- Shallow	0 (0.0%)	1 (6.7%)	1 (3.7%)	
- missing	1	0	1	
Slitlamp - Lens				
- Normal	4 (30.8%)	7 (46.7%)	11 (39.3%)	0.3951 *[3]
- Posterior cataract	1 (7.7%)	3 (20.0%)	4 (14.3%)	
- Pseudophakic	3 (23.1%)	1 (6.7%)	4 (14.3%)	
- Other	5 (38.5%)	3 (20.0%)	8 (28.6%)	
- Pseudophakic+Other	0 (0.0%)	1 (6.7%)	1 (3.6%)	
Slitlamp - Vitreous cavity				
- Normal	10 (76.9%)	13 (86.7%)	23 (82.1%)	0.3833 *[3]
- Cloudy	2 (15.4%)	0 (0.0%)	2 (7.1%)	
- Other	1 (7.7%)	2 (13.3%)	3 (10.7%)	
Slitlamp - Retinal attachment				
- Completely attached	13 (100.0%)	15 (100.0%)	28 (100.0%)	
Slitlamp - Retinal abnormalities				
- Pucker	0 (0.0%)	1 (7.1%)	1 (3.8%)	0.7973 *[3]
- Edema	0 (0.0%)	1 (7.1%)	1 (3.8%)	
- Subret.hemorrhage	2 (16.7%)	2 (14.3%)	4 (15.4%)	
- Subret.fibrosis	0 (0.0%)	1 (7.1%)	1 (3.8%)	
- No abnorm.	6 (50.0%)	3 (21.4%)	9 (34.6%)	
- Other	3 (25.0%)	3 (21.4%)	6 (23.1%)	
- Subret.hemorr.+fibrosis	0 (0.0%)	1 (7.1%)	1 (3.8%)	
- Subret.hemorr.+other	0 (0.0%)	1 (7.1%)	1 (3.8%)	
- No abnorm.+other	0 (0.0%)	1 (7.1%)	1 (3.8%)	
- Edema+subret.hemorr.+other	1 (8.3%)	0 (0.0%)	1 (3.8%)	
- missing	1	1	2	
Slitlamp - Foveal position				
- Within the defect area	12 (100.0%)	13 (100.0%)	25 (100.0%)	
- missing	1	1	2	
Slitlamp - Recurrence				
- no	10 (100.0%)	10 (100.0%)	20 (100.0%)	
- missing	3	5	8	

*[3] = Fisher's Exact Test

The results from measuring the intraocular pressure (tonometry) shows Table A 5.

Table A 5: Study eye: Tonometry (entry examination).

	Treatment N=13	Control N=15	Total N=28	p-value
Tonometry				
- N	13	15	28	0.8893 *[1]
- Mean +/- SD	13.8 +/- 3.7	13.4 +/- 3.1	13.6 +/-3.3	
- p5, p25, p75, p95	8.0, 11.0, 17.0, 18.0	9.0, 11.0, 15.0, 19.0	8.0, 11.0, 16.5, 18.0	
- Median	14.0	13.0	13.0	
- Min, Max	8.0, 18.0	9.0, 19.0	8.0, 19.0	
- 95% CI Mean	[11.5;16.0]	[11.7;15.1]	[12.3;14.9]	
- 95% CI Median	[11.0;18.0]	[11.0;15.0]	[12.0;16.0]	

*[1] = U-Test

Table A 6 shows the Cyclorotation (median of the six measurements for incyclorotation and excyclorotation) for the study eye.

Table A 6: Study eye: Cyclorotation (Entry Examination).

	Treatment N=13	Control N=15	Total N=28	p-value
Baseline: Study Eye - Median monocular subjective cyclorotation				
- N	13	15	28	0.5987 *[1]
- Mean +/- SD	-0.3 +/- 1.2	0.1 +/- 1.4	-0.1 +/-1.3	
- p5, p25, p75, p95	-3.5, 0.0, 0.0, 1.0	-2.5, 0.0, 1.0, 2.5	-2.5, 0.0, 0.3, 2.5	
- Median	0.0	0.0	0.0	
- Min, Max	-3.5, 1.0	-2.5, 2.5	-3.5, 2.5	
- 95% CI Mean	[-1.1;0.4]	[-0.6;0.8]	[-0.6;0.4]	
- 95% CI Median	[-0.5;0.5]	[0.0;1.0]	[0.0;0.0]	

*[1] = U-Test

The results of the examination of the study eye show no difference between both groups in the

- grading of cataract according LOCS III,
- examination of differential light sensitivity in the visual field,
- slitlamp examinations,
- tonometry and
- cyclorotation.

11.2.2 Fellow Eye

In this part results of the further examinations of the fellow eye at entry examination are presented. Table A 7 shows the grading of cataract according to the Lens Opacities Classification System III. The LOCS III contains an expanded set of standards. It consists of six slit-lamp images for grading nuclear color (NC) and nuclear opalescence (NO), five retroillumination images for grading cortical cataract (C), and five retroillumination images for grading posterior subcapsular (P) cataract.

Table A 7: Fellow eye: Grading of cataract according to LOCS III (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Grading of cataract – NO				
- N	11	14	25	0.2794 *[1]
- Mean +/- SD	1.3 +/- 1.0	0.8 +/- 0.7	1.0 +/-0.9	
- p5, p25, p75, p95	0.2, 0.3, 2.0, 3.5	0.2, 0.2, 1.5, 2.0	0.2, 0.3, 1.5, 2.0	
- Median	1.5	0.4	1.0	
- Min, Max	0.2, 3.5	0.2, 2.0	0.2, 3.5	
- 95% CI Mean	[0.6;2.0]	[0.4;1.3]	[0.7;1.4]	
- 95% CI Median	[0.3;2.0]	[0.2;2.0]	[0.3;1.5]	
Grading of cataract - NC				
- N	11	14	25	0.3612 *[1]
- Mean +/- SD	1.3 +/- 1.1	1.0 +/- 1.0	1.1 +/-1.0	
- p5, p25, p75, p95	0.2, 0.3, 2.0, 3.5	0.2, 0.2, 2.0, 3.0	0.2, 0.3, 2.0, 3.0	
- Median	1.0	0.4	1.0	
- Min, Max	0.2, 3.5	0.2, 3.0	0.2, 3.5	
- 95% CI Mean	[0.6;2.1]	[0.4;1.5]	[0.7;1.6]	
- 95% CI Median	[0.3;2.5]	[0.2;2.0]	[0.3;2.0]	
Grading of cataract - C				
- N	11	14	25	0.7805 *[1]
- Mean +/- SD	0.7 +/- 1.0	0.8 +/- 1.0	0.8 +/-1.0	
- p5, p25, p75, p95	0.0, 0.1, 1.0, 3.5	0.1, 0.1, 1.0, 3.0	0.1, 0.1, 1.0, 3.0	
- Median	0.2	0.3	0.2	
- Min, Max	0.0, 3.5	0.1, 3.0	0.0, 3.5	
- 95% CI Mean	[0.0;1.4]	[0.2;1.4]	[0.4;1.2]	
- 95% CI Median	[0.1;1.0]	[0.1;2.5]	[0.2;1.0]	
Grading of cataract - P				
- N	11	14	25	0.8587 *[1]
- Mean +/- SD	0.2 +/- 0.3	0.4 +/- 0.8	0.3 +/-0.6	
- p5, p25, p75, p95	0.0, 0.1, 0.3, 1.0	0.1, 0.1, 0.2, 3.0	0.1, 0.1, 0.2, 1.0	
- Median	0.1	0.1	0.1	
- Min, Max	0.0, 1.0	0.1, 3.0	0.0, 3.0	
- 95% CI Mean	[0.0;0.4]	[-0.0;0.9]	[0.1;0.6]	
- 95% CI Median	[0.1;0.3]	[0.1;0.4]	[0.1;0.2]	

*[1] = U-Test

Table A 8 shows the assessment of the cyclorotation (median of the six measurements for incyclorotation and excyclorotation) in the fellow eye at the entry examination.

Table A 8: Fellow eye: Cyclorotation (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
Baseline: Fellow Eye - Median monocular subjective cyclorotation				
- N	13	12	25	0.5576 *[1]
- Mean +/- SD	-0.6 +/- 1.2	-0.5 +/- 1.6	-0.5 +/-1.4	
- p5, p25, p75, p95	-3.0, -1.0, 0.0, 1.0	-5.0, -0.5, 0.0, 1.5	-3.0, -1.0, 0.0, 1.0	
- Median	0.0	0.0	0.0	
- Min, Max	-3.0, 1.0	-5.0, 1.5	-5.0, 1.5	
- 95% CI Mean	[-1.3;0.1]	[-1.4;0.5]	[-1.1;0.0]	
- 95% CI Median	[-1.0;0.0]	[-1.0;0.0]	[-1.0;0.0]	

*[1] = U-Test

The results show no differences between both groups in the grading of cataract according LOCS III in the fellow eye and in the cyclorotation in the fellow eye.

11.2.3 Details of the Medical History

In this part details of the medical history are listed: diseases, diagnoses, hypersensitivities, and operations. There were other diseases of the cardiovascular system documented in five patients, there were diagnoses for the gastrointestinal system documented in six patients (Table A 9).

Table A 9: Listing of diseases documented for the cardiovascular system and diagnoses for the gastrointestinal system.

Patient Identification	Card. system other Diagnosis	Gastro. system Diagnosis
001/11/female/66/Translocation		
002/11/male/83/Control		
003/01/female/65/Translocation		
004/11/female/75/Translocation		
005/11/female/77/Control		COLONECTOMY (RADIATION BURNS) 1997-8
006/11/female/79/Translocation		
007/11/female/73/Control		
008/11/male/58/Control	OESOPHAGEAL VARICES FROM LIVER DISEASE 15 YEARS AGO	
009/01/female/76/Control	CASUAL ARHYTHMIA	
010/11/male/73/Translocation		
011/01/female/69/Control		
012/01/female/74/Translocation		
013/01/female/79/Control		CHRON. GASTRITIS, HIATUSHERNIE,DIVERTIKULOSE
014/11/female/76/Translocation		ACID REFLUX
015/01/female/62/Translocation		
016/01/male/66/Control		
017/01/female/71/Translocation		
018/11/female/66/Translocation		
019/01/female/69/Control		
020/01/female/74/Control		ULCUS VENTRICULI
021/11/female/65/Control		
022/01/male/82/Translocation		
023/01/female/78/Translocation	KHK	ESOPHAGITIS, REFLUX
024/11/female/78/Control		
025/01/female/79/Control	CORONARY HEART DISEASE	
026/01/male/64/Control	CIRCULATORY DISORDER LEFT LEG	
027/01/male/67/Control		Z.N. ENDOGASTRITIS 1955
028/11/female/68/Translocation		

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

Table A 10 shows a listing of diagnoses of the bronchopulmonary system, diagnoses for other diseases of Endocronology/Metabolism, diabetes, hyperlipidemia.

Table A 10: Listing of diagnoses of the bronchopulmonary system, other diseases of Endocronology/Metabolism, diagnosed diabetes mellitus, hyperlipidemia.

Patient Identification	Broncho. system Diagnosis	Diabetes Mellitus	DM since	Hyperlipidemia	Endo./Metab. others Diagnosis
001/11/female/66/Translocation		no		no	
002/11/male/83/Control		no		no	
003/01/female/65/Translocation	V.A. ASTHMA / RAUCHER	no		yes	SD-VERGROESSERUNG OHNE DYSFUNKTION
004/11/female/75/Translocation	ASTHMA ON INHALER.	no		no	
005/11/female/77/Control		no		no	OVARIAN CANCER OOPHORECTOMY AND RADIOTHERAPY 1960'S
006/11/female/79/Translocation		no		no	HYPERTHYRODISM, RADIOACTIVE IODINE
007/11/female/73/Control		yes	1987	no	
008/11/male/58/Control		no		no	
009/01/female/76/Control		no		no	
010/11/male/73/Translocation		no		no	
011/01/female/69/Control		no		no	HYPERTHYREOIDISM SINCE 1970
012/01/female/74/Translocation		no		no	
013/01/female/79/Control		no		yes	
014/11/female/76/Translocation		no		no	HYPOTHYROID
015/01/female/62/Translocation		no		no	HYPERTHYROIDISM
016/01/male/66/Control		yes	1987	yes	HYPERURICEMIA
017/01/female/71/Translocation		no		no	
018/11/female/66/Translocation		no		no	
019/01/female/69/Control	BRONCHITIS	no		yes	
020/01/female/74/Control	BRONCHIAL ASTHMA	no		no	
021/11/female/65/Control		no		no	
022/01/male/82/Translocation		no		yes	
023/01/female/78/Translocation		no		yes	HYPOTHYROIDISM
024/11/female/78/Control	SMOKER'S COUGH	no		no	
025/01/female/79/Control		no		no	
026/01/male/64/Control		no		no	
027/01/male/67/Control		no		no	
028/11/female/68/Translocation		no		no	

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

Table A 11 shows a listing of other diseases than asked in the CRF and known hypersensitivities.

Table A 11: Listing of other diseases than asked in the CRF and known hypersensitivities.

Patient Identification	Med. History Other Diagnosis	Hypersensitivities	Hypersensitivities specify
001/11/female/66/Translocation		yes	CODEINE AND CODEINE DERIVATIVES
002/11/male/83/Control		no	
003/01/female/65/Translocation		yes	SONNENALLERGIE
004/11/female/75/Translocation		no	
005/11/female/77/Control		yes	MORPHINE
006/11/female/79/Translocation		no	
007/11/female/73/Control		no	
008/11/male/58/Control		no	
009/01/female/76/Control		no	
010/11/male/73/Translocation		no	
011/01/female/69/Control		no	
012/01/female/74/Translocation		no	
013/01/female/79/Control	MULTIPLE FRACTURES	no	
014/11/female/76/Translocation	HYPOTHYRODISM	yes	CODEINE
015/01/female/62/Translocation		yes	NICKELSULFAT, KOBALTSULFAT, PALLADIUMCHLORID
016/01/male/66/Control		no	
017/01/female/71/Translocation	PALSY OF N. PERONAEUS	no	
018/11/female/66/Translocation		no	
019/01/female/69/Control	PSORIASIS	yes	ALLERGIE TO PLASTER
020/01/female/74/Control	ARTHROSIS, ECZEMA(SKIN)	no	
021/11/female/65/Control	ARTHRITIS IN BOTH FEET AND KNEES	no	
022/01/male/82/Translocation		no	
023/01/female/78/Translocation		yes	FAG (FLUORESZEN-ANGIOGRAPHIE)
024/11/female/78/Control		no	
025/01/female/79/Control		no	
026/01/male/64/Control	DEGENERATION OF SPINE	no	
027/01/male/67/Control	DISKPROLAPSE 2000	no	
028/11/female/68/Translocation		no	

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

Table A 12 shows a listing of severe operations (17 patients).

Table A 12: Listing of severe operations.

Patient Identification	Severe Operations	Operations
001/11/female/66/Translocation	yes	CHOLECYSTECTOMY (1971) DILATATIONANDCURRETTAGE (1978) HALUXVALGUS (1992)
002/11/male/83/Control	no	
003/01/female/65/Translocation	yes	UTERUSENTFERNUNG (1976)
004/11/female/75/Translocation	no	
005/11/female/77/Control	yes	OOPHORECTOMY1960'S (1960) HYSTEROTOMY1960'S (1960) HIPREPLACEMENT1999 (1999) COLONECTOMY1997-8 (1997)
006/11/female/79/Translocation	yes	HYSTERECTOMY (1962)
007/11/female/73/Control	yes	HYSTERECTOMY (1960)
008/11/male/58/Control	no	
009/01/female/76/Control	yes	BREASTCANCER,RADIATION+RESECTIONDEXTER (1970) BREASTCANCER,RADIATION+RESECTIONDEXTER (1995)
010/11/male/73/Translocation	no	
011/01/female/69/Control	yes	GALLBLADDEROP (1965) UTERECTOMY (1970)
012/01/female/74/Translocation	yes	TOTAL-OPBYCA(4CHEMO/4RADIATIO) (1990) RE-CA,RE-OP (1995)
013/01/female/79/Control	yes	LEFTWRISTFRACTURE (1999)
014/11/female/76/Translocation	yes	HYSTERECTOMY (1982)
015/01/female/62/Translocation	no	
016/01/male/66/Control	no	
017/01/female/71/Translocation	yes	INTERVERTEBRALDISCS (1990) BENIGNTUMOR(LEFTCERVIX) (2001)
018/11/female/66/Translocation	yes	HYSTERECTOMYCERVICALCANCER (1996)
019/01/female/69/Control	yes	RESECTIONGALLBLADDER (1973) RESECTIONUTERUS (1983) RESECTIONOVARIAN (1998)
020/01/female/74/Control	yes	HIP-OP (1993) HYSTERECTOMY (1972)
021/11/female/65/Control	no	
022/01/male/82/Translocation	yes	BYPASS-OP (1998)
023/01/female/78/Translocation	no	
024/11/female/78/Control	yes	OPERATION(BENIGNTUMOUR)HYSTERECTOMY25YEARSAGO (1979)
025/01/female/79/Control	no	
026/01/male/64/Control	no	
027/01/male/67/Control	yes	PLASTICSURGERYINTHEAREAOFTHEHEAD (1971) GASTRICRUPTURE (1980)
028/11/female/68/Translocation	no	

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

11.2.4Eye specific Quality of Life

Table A 13 shows the description of the 12 subs scales of the NEI VFQ score.

Table A 13: Subscales of the Visual Functioning Questionnaire (entry examination).

	Treatment N=13	**Control N=15**	**Total N=28**	**p-value**
General Health				
- N	13	15	28	0.0933 *[1]
- Mean +/- SD	51.9 +/- 16.0	40.0 +/- 18.4	45.5 +/-18.1	
- p5, p25, p75, p95	25.0, 50.0, 50.0, 75.0	0.0, 25.0, 50.0, 75.0	25.0, 25.0, 50.0, 75.0	
- Median	50.0	50.0	50.0	
- Min, Max	25.0, 75.0	0.0, 75.0	0.0, 75.0	
- 95% CI Median	[50.0;75.0]	[25.0;50.0]	[50.0;50.0]	
General Vision				
- N	13	15	28	0.1350 *[1]
- Mean +/- SD	46.2 +/- 18.9	36.0 +/- 13.5	40.7 +/-16.8	
- p5, p25, p75, p95	20.0, 40.0, 60.0, 80.0	20.0, 20.0, 40.0, 60.0	20.0, 20.0, 60.0, 60.0	
- Median	40.0	40.0	40.0	
- Min, Max	20.0, 80.0	20.0, 60.0	20.0, 80.0	
- 95% CI Median	[20.0;60.0]	[20.0;40.0]	[40.0;40.0]	
Ocular Pain				
- N	13	15	28	0.1408 *[1]
- Mean +/- SD	83.7 +/- 19.4	90.8 +/- 17.3	87.5 +/-18.3	
- p5, p25, p75, p95	37.5, 87.5, 100.0, 100.0	37.5, 87.5, 100.0, 100.0	37.5, 87.5, 100.0, 100.0	
- Median	87.5	100.0	93.8	
- Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0	
- 95% CI Median	[75.0;100.0]	[87.5;100.0]	[87.5;100.0]	
Near Activities				
- N	13	15	28	0.6570 *[1]
- Mean +/- SD	35.9 +/- 15.4	33.3 +/- 16.1	34.5 +/-15.5	
- p5, p25, p75, p95	16.7, 25.0, 50.0, 58.3	8.3, 16.7, 41.7, 66.7	16.7, 20.8, 41.7, 58.3	
- Median	33.3	33.3	33.3	
- Min, Max	16.7, 58.3	8.3, 66.7	8.3, 66.7	
- 95% CI Median	[16.7;50.0]	[16.7;41.7]	[25.0;41.7]	
Distance Activities				
- N	13	15	28	0.4568 *[1]
- Mean +/- SD	41.7 +/- 27.4	33.3 +/- 18.1	37.2 +/-22.8	
- p5, p25, p75, p95	8.3, 25.0, 50.0, 91.7	8.3, 16.7, 41.7, 75.0	8.3, 20.8, 50.0, 83.3	
- Median	41.7	25.0	33.3	
- Min, Max	8.3, 91.7	8.3, 75.0	8.3, 91.7	
- 95% CI Median	[8.3;66.7]	[16.7;41.7]	[25.0;50.0]	
Vision Specific: Social Functioning				
- N	13	15	28	0.5729 *[1]
- Mean +/- SD	46.2 +/- 34.0	35.8 +/- 22.6	40.6 +/-28.4	
- p5, p25, p75, p95	0.0, 12.5, 75.0, 100.0	0.0, 25.0, 50.0, 87.5	0.0, 25.0, 62.5, 87.5	
- Median	37.5	25.0	25.0	
- Min, Max	0.0, 100.0	0.0, 87.5	0.0, 100.0	
- 95% CI Median	[12.5;75.0]	[25.0;50.0]	[25.0;62.5]	
Vision Specific: Mental Health				
- N	13	15	28	0.7458 *[1]
- Mean +/- SD	37.0 +/- 22.6	32.5 +/- 19.8	34.6 +/-20.9	
- p5, p25, p75, p95	6.3, 25.0, 56.3, 81.3	0.0, 18.8, 43.8, 68.8	6.3, 18.8, 46.9, 68.8	
- Median	31.3	43.8	34.4	
- Min, Max	6.3, 81.3	0.0, 68.8	0.0, 81.3	
- 95% CI Median	[12.5;62.5]	[18.8;43.8]	[25.0;43.8]	

	Treatment N=13	Control N=15	Total N=28	p-value
Vision Specific: Role Difficulties				
- N	13	15	28	0.8877 *[1]
- Mean +/- SD	51.0 +/- 27.2	54.2 +/- 23.0	52.7 +/-24.6	
- p5, p25, p75, p95	0.0, 37.5, 62.5, 100.0	0.0, 37.5, 75.0, 87.5	0.0, 37.5, 75.0, 87.5	
- Median	50.0	50.0	50.0	
- Min, Max	0.0, 100.0	0.0, 87.5	0.0, 100.0	
- 95% CI Median	[25.0;75.0]	[37.5;75.0]	[50.0;62.5]	
Vision Specific: Dependency				
- N	13	15	28	0.8713 *[1]
- Mean +/- SD	51.3 +/- 32.1	53.3 +/- 35.0	52.4 +/-33.1	
- p5, p25, p75, p95	0.0, 25.0, 75.0, 100.0	0.0, 16.7, 83.3, 100.0	0.0, 20.8, 79.2, 100.0	
- Median	50.0	58.3	54.2	
- Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0	
- 95% CI Median	[16.7;83.3]	[16.7;83.3]	[41.7;75.0]	
Driving				
- N	1	2	3	1.0000 *[1]
- Mean +/- SD	50.0 +/- .	43.8 +/- 8.8	45.8 +/-7.2	
- p5, p25, p75, p95	50.0, 50.0, 50.0, 50.0	37.5, 37.5, 50.0, 50.0	37.5, 37.5, 50.0, 50.0	
- Median	50.0	43.8	50.0	
- Min, Max	50.0, 50.0	37.5, 50.0	37.5, 50.0	
- 95% CI Median	[.;.]	[37.5;50.0]	[37.5;50.0]	
Color Vision				
- N	13	15	28	0.9230 *[1]
- Mean +/- SD	73.1 +/- 29.7	73.3 +/- 25.8	73.2 +/-27.2	
- p5, p25, p75, p95	25.0, 50.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0	
- Median	75.0	75.0	75.0	
- Min, Max	25.0, 100.0	25.0, 100.0	25.0, 100.0	
- 95% CI Median	[50.0;100.0]	[50.0;100.0]	[50.0;100.0]	
Peripheral Vision				
- N	13	14	27	0.3545 *[1]
- Mean +/- SD	80.8 +/- 20.8	71.4 +/- 25.7	75.9 +/-23.5	
- p5, p25, p75, p95	50.0, 75.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0	50.0, 50.0, 100.0, 100.0	
- Median	75.0	75.0	75.0	
- Min, Max	50.0, 100.0	25.0, 100.0	25.0, 100.0	
- 95% CI Median	[50.0;100.0]	[50.0;100.0]	[50.0;100.0]	

*[1] = U-Test

The data show no difference between both groups.

11.3 Performance of the Macular Translocation Surgery and Muscular Counterrotation Surgery

Table A 14 and Table A 15 give detailed information about the performance of the macular translocation surgery. Macular translocation surgery was performed in 10 of the 13 patients randomized to the MT group.

Table A 14: Details of the Macular Translocation Surgery 1/2.

Patient Identification	Surgery [min]	Retinal detach. [min]	Anaesthesia [min]	Detachment achivied by	Transloc.	No. retinotomies	BSS appl. [min]	BSS modific.?	Solution	Hemorrhage	Membrane adhered?	IOL implant.?	Counter rot.?	Anaesth. probl.?
001/11/female/66/Translocation	77	50	103	Transvitreal approach	Upward	1	13	no		moderate	no	yes	no	no
003/01/female/65/Translocation	130	50	150	Transvitreal approach	Upward	3	110	yes	ALCON BSS PLUS	moderate	no	yes	no	no
004/11/female/75/Translocation	95	45	120	Transvitreal approach	Upward	1	5	yes	5 FU + HEPARIN	none	yes	yes	no	no
006/11/female/79/Translocation	110	47	135	Transvitreal approach	Upward	1	8	no		moderate	no	yes	no	yes
010/11/male/73/Translocation	117	16	135	Transvitreal approach	Upward	1	16	yes	5FU AND HEPARIN	moderate	no	yes	no	no
014/11/female/76/Translocation	145	73	155	Transvitreal approach	Upward	2	15	yes	5FU AND HEPARIN	none	yes	no	no	no
017/01/female/71/Translocation	90	40	130	Transvitreal approach	Upward	1	7	yes	ADRENALIN	moderate	yes	no	no	yes
018/11/female/66/Translocation	120	54	145	Transvitreal approach	Upward	1	100	yes	HEPARIN, 5FU	moderate	no	yes	no	no
023/01/female/78/Translocation	120	30	160	Combined	Downward	2	16	no		none	yes	no	no	no
028/11/female/68/Translocation	90	52	105	Transvitreal approach	Upward	1	10	yes	5 FU AND HEPARIN	moderate	no	yes	no	no

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

Table A 15: Details of the Macular Translocation Surgery 2/2.

Patient Identification	Problem	Compl.?	Complication
001/11/female/66/Translocation		no	
003/01/female/65/Translocation		yes	IOL DISLOCATION
004/11/female/75/Translocation		no	
006/11/female/79/Translocation	FEW ECTOPIC BEATS WERE NOTED, PATIENT WAS MONITORED OVERNIGHT	no	
010/11/male/73/Translocation		no	
014/11/female/76/Translocation		no	
017/01/female/71/Translocation	VOMETING	yes	ZONULOLYSE IRISDEFECT 10H
018/11/female/66/Translocation		no	
023/01/female/78/Translocation		yes	BIG PIGMENT EPITHELIUM DETACHMENT + DETACHED RETINA, DOWN ROTAT. 80-90 BEC. OF LOSS OF PIGMENT EPITH
028/11/female/68/Translocation		no	

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

Table A 16 shows details of the performance of the muscular counterrotation surgery. In all of these patients the macular translocation surgery was performed as upward translocation. For Patid = 23, no information about the muscular counterrotation surgery is available.

Table A 16: Characteristics of the Muscular Counterrotation Surgery.

Identification	Date of Surgery	Eye	Oil removal?	Obj. cyclorot.	Rec. sup.obl.?	mm	full tendon	ant. margin	Adv. inf.obl.?	mm	full tendon	ant. margin	Downw. int.rect.?	mm	Upw. ext.rect.?	mm	Transp. sup.obl.?	mm
001/11/female/66/Translocation	16/01/2003	study	yes	45	no				yes	14.0			no		no		no	
003/01/female/65/Translocation	27/01/2003	study	yes	30	no				yes	16.0	yes		yes	10.0	yes	10.0	yes	22.0
004/11/female/75/Translocation	20/02/2003	study	yes	60	no				no				no		no		yes	4.0
006/11/female/79/Translocation	10/04/2003	study	yes	45					yes	5.0	yes						yes	5.0
010/11/male/73/Translocation	17/07/2003	study	yes	85	no		yes		yes				no		no		no	
011/01/female/69/Control	01/09/2003	study	yes		no				yes	12.0		yes	yes	8.0	yes	8.0	yes	4.0
014/11/female/76/Translocation	18/09/2003	study	yes		yes				yes								yes	5.0
017/01/female/71/Translocation	06/11/2003	study	yes	41	no				yes	12.0		yes	yes	8.0	yes	8.0	yes	4.0
018/11/female/66/Translocation	03/06/2004	study	yes	30	yes	7.0	yes		yes	7.0	yes		no		no		yes	
023/01/female/78/Translocation	20/04/2004	ND	no	NA														
028/11/female/68/Translocation	23/09/2004	study		45	yes				yes				no		no		no	

The column 'Patient Identification' comprises of 'Random.No./Site No./Sex/Age/Group'

11.4 Control Examinations: Further Results

In this part the details of the further examinations during the follow up phase are presented:

- fundus classification (study eye)
- RPE-detachment, subretinal extrafoveal hemorrhage, other results (study eye)
- grading of cataract according to the LOCS III (study eye and fellow eye)
- results of the examination of differential light sensitivity in the visual field (Goldman perimetry) (study eye)
- results from the slitlamp examination (study eye)
- results from measuring the intraocular pressure (tonometry) (study eye)
- results from cyclorotation and binocular vision.

Furthermore, the assessment of the study eye and the fellow eye is presented (refraction).

Table A 17 shows the subfoveal choroidal neovascular membrane classification (fundus classification), in the study eye, Table A 18 shows the results of the macula examination (RPE detachment, subretinal extrafoveal hemorrhage).

Table A 17: Study eye: Fundus classification (control examinations in week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Fundus classification			
- occult	6 (85.7%)	8 (66.7%)	14 (73.7%)
- mixed (<50%classic)	1 (14.3%)	4 (33.3%)	5 (26.3%)
- missing	5	2	7
Week 26: Fundus classification			
- occult	10 (100.0%)	8 (66.7%)	18 (81.8%)
- mixed (<50%classic)	0 (0.0%)	4 (33.3%)	4 (18.2%)
- missing	1	2	3
Week 38: Fundus classification			
- occult	7 (70.0%)	7 (63.6%)	14 (66.7%)
- mixed (<50%classic)	3 (30.0%)	4 (36.4%)	7 (33.3%)
- missing	1	3	4
Week 52: Fundus classification			
- occult	4 (44.4%)	8 (66.7%)	12 (57.1%)
- mixed (<50%classic)	5 (55.6%)	4 (33.3%)	9 (42.9%)
- missing	1	0	1
Week 104: Fundus classification			
- occult	5 (62.5%)	9 (75.0%)	14 (70.0%)
- mixed (<50%classic)	3 (37.5%)	3 (25.0%)	6 (30.0%)
- missing	1	1	2

Table A 18: Study eye: RPE-detachment and subretinal extrafoveal hemorrhage (control examinations in week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: RPE-detachment			
- no	8 (100.0%)	8 (66.7%)	16 (80.0%)
- yes	0 (0.0%)	4 (33.3%)	4 (20.0%)
- missing	5	2	7
Week 12: Subretinal extrafoveal hemorrhage			
- no	7 (87.5%)	6 (50.0%)	13 (65.0%)
- yes	1 (12.5%)	6 (50.0%)	7 (35.0%)
- missing	5	2	7
Week 26: RPE-detachment			
- no	12 (100.0%)	9 (75.0%)	21 (87.5%)
- yes	0 (0.0%)	3 (25.0%)	3 (12.5%)
- missing	1	2	3
Week 26: Subretinal extrafoveal hemorrhage			
- no	12 (100.0%)	6 (54.5%)	18 (78.3%)
- yes	0 (0.0%)	5 (45.5%)	5 (21.7%)
- missing	1	2	3
Week 38: RPE-detachment			
- no	12 (100.0%)	7 (70.0%)	19 (86.4%)
- yes	0 (0.0%)	3 (30.0%)	3 (13.6%)
- missing	1	3	4
Week 38: Subretinal extrafoveal hemorrhage			
- no	10 (83.3%)	6 (54.5%)	16 (69.6%)
- yes	2 (16.7%)	5 (45.5%)	7 (30.4%)
- missing	1	3	4
Week 52: RPE-detachment			
- no	12 (100.0%)	11 (78.6%)	23 (88.5%)
- yes	0 (0.0%)	3 (21.4%)	3 (11.5%)
- missing	1	0	1
Week 52: Subretinal extrafoveal hemorrhage			
- no	12 (100.0%)	10 (71.4%)	22 (84.6%)
- yes	0 (0.0%)	4 (28.6%)	4 (15.4%)
- missing	1	0	1
Week 104: RPE-detachment			
- no	11 (100.0%)	12 (92.3%)	23 (95.8%)
- yes	0 (0.0%)	1 (7.7%)	1 (4.2%)
- missing	1	1	2
Week 104: Subretinal extrafoveal hemorrhage			
- no	11 (100.0%)	11 (84.6%)	22 (91.7%)
- yes	0 (0.0%)	2 (15.4%)	2 (8.3%)
- missing	1	1	2

Table A 19 respectively Table A 20 shows the grading of cataract according to the Lens Opacities Classification System III for the study eye respectively for the fellow eye. The LOCS III contains an expanded set of standards It consists of six slit-lamp images for grading nuclear color (NC) and nuclear

opalescence (NO), five retroillumination images for grading cortical cataract (C), and five retroillumination images for grading posterior subcapsular (P) cataract.

Table A 19: Study eye: Grading of cataract according to LOCS III (control examinations in week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Study Eye - NO			
- N		11	11
- Mean +/- SD		1.0 +/- 0.9	1.0 +/-0.9
- p5, p25, p75, p95		0.2, 0.2, 1.5, 2.5	0.2, 0.2, 1.5, 2.5
- Median		0.4	0.4
- Min, Max		0.2, 2.5	0.2, 2.5
- 95% CI Mean		[0.4;1.6]	[0.4;1.6]
- 95% CI Median		[0.2;2.5]	[0.2;2.5]
Week 12: Study Eye - NC			
- N		11	11
- Mean +/- SD		1.0 +/- 0.9	1.0 +/-0.9
- p5, p25, p75, p95		0.2, 0.3, 1.5, 2.5	0.2, 0.3, 1.5, 2.5
- Median		0.4	0.4
- Min, Max		0.2, 2.5	0.2, 2.5
- 95% CI Mean		[0.4;1.6]	[0.4;1.6]
- 95% CI Median		[0.3;2.5]	[0.3;2.5]
Week 12: Study Eye - C			
- N		11	11
- Mean +/- SD		0.8 +/- 1.0	0.8 +/-1.0
- p5, p25, p75, p95		0.1, 0.1, 1.0, 3.0	0.1, 0.1, 1.0, 3.0
- Median		0.2	0.2
- Min, Max		0.1, 3.0	0.1, 3.0
- 95% CI Mean		[0.1;1.5]	[0.1;1.5]
- 95% CI Median		[0.1;2.5]	[0.1;2.5]
Week 12: Study Eye - P			
- N		11	11
- Mean +/- SD		0.4 +/- 0.9	0.4 +/-0.9
- p5, p25, p75, p95		0.1, 0.1, 0.2, 3.0	0.1, 0.1, 0.2, 3.0
- Median		0.1	0.1
- Min, Max		0.1, 3.0	0.1, 3.0
- 95% CI Mean		[-0.2;1.0]	[-0.2;1.0]
- 95% CI Median		[0.1;0.5]	[0.1;0.5]
Week 26: Study Eye - NO			
- N	1	11	12
- Mean +/- SD	0.3 +/- .	1.1 +/- 0.9	1.1 +/-0.8
- p5, p25, p75, p95	0.3, 0.3, 0.3, 0.3	0.2, 0.3, 2.0, 2.5	0.2, 0.3, 1.8, 2.5
- Median	0.3	1.5	1.0
- Min, Max	0.3, 0.3	0.2, 2.5	0.2, 2.5
- 95% CI Mean	[.;.]	[0.6;1.7]	[0.5;1.6]
- 95% CI Median	[.;.]	[0.3;2.0]	[0.3;2.0]
Week 26: Study Eye - NC			
- N	1	11	12
- Mean +/- SD	0.3 +/- .	1.2 +/- 1.0	1.2 +/-1.0
- p5, p25, p75, p95	0.3, 0.3, 0.3, 0.3	0.2, 0.3, 2.0, 3.0	0.2, 0.3, 1.8, 3.0
- Median	0.3	1.5	1.0
- Min, Max	0.3, 0.3	0.2, 3.0	0.2, 3.0
- 95% CI Mean	[.;.]	[0.6;1.9]	[0.5;1.8]
- 95% CI Median	[.;.]	[0.3;2.5]	[0.3;2.0]
Week 26: Study Eye - C			

	Treatment N=13	Control N=15	Total N=28
- N	1	11	12
- Mean +/- SD	0.2 +/- .	0.9 +/- 1.0	0.8 +/-1.0
- p5, p25, p75, p95	0.2, 0.2, 0.2, 0.2	0.1, 0.1, 1.0, 3.0	0.1, 0.2, 1.0, 3.0
- Median	0.2	0.4	0.3
- Min, Max	0.2, 0.2	0.1, 3.0	0.1, 3.0
- 95% CI Mean	[.;.]	[0.2;1.5]	[0.2;1.4]
- 95% CI Median	[.;.]	[0.1;2.5]	[0.1;1.0]
Week 26: Study Eye - P			
- N	1	11	12
- Mean +/- SD	0.2 +/- .	0.5 +/- 0.9	0.4 +/-0.8
- p5, p25, p75, p95	0.2, 0.2, 0.2, 0.2	0.1, 0.1, 0.2, 3.0	0.1, 0.1, 0.2, 3.0
- Median	0.2	0.1	0.1
- Min, Max	0.2, 0.2	0.1, 3.0	0.1, 3.0
- 95% CI Mean	[.;.]	[-0.1;1.1]	[-0.1;1.0]
- 95% CI Median	[.;.]	[0.1;1.0]	[0.1;0.2]
Week 38: Study Eye - NO			
- N	1	10	11
- Mean +/- SD	0.3 +/- .	1.3 +/- 0.9	1.2 +/-0.9
- p5, p25, p75, p95	0.3, 0.3, 0.3, 0.3	0.3, 0.4, 2.0, 2.5	0.3, 0.4, 2.0, 2.5
- Median	0.3	1.0	1.0
- Min, Max	0.3, 0.3	0.3, 2.5	0.3, 2.5
- 95% CI Mean	[.;.]	[0.7;1.9]	[0.6;1.8]
- 95% CI Median	[.;.]	[0.4;2.5]	[0.4;2.5]
Week 38: Study Eye - NC			
- N	1	10	11
- Mean +/- SD	0.3 +/- .	1.4 +/- 1.0	1.3 +/-1.0
- p5, p25, p75, p95	0.3, 0.3, 0.3, 0.3	0.3, 0.4, 2.0, 3.0	0.3, 0.4, 2.0, 3.0
- Median	0.3	1.0	1.0
- Min, Max	0.3, 0.3	0.3, 3.0	0.3, 3.0
- 95% CI Mean	[.;.]	[0.7;2.0]	[0.6;1.9]
- 95% CI Median	[.;.]	[0.4;2.5]	[0.4;2.5]
Week 38: Study Eye - C			
- N	1	10	11
- Mean +/- SD	0.2 +/- .	0.9 +/- 1.0	0.8 +/-0.9
- p5, p25, p75, p95	0.2, 0.2, 0.2, 0.2	0.1, 0.1, 1.0, 3.0	0.1, 0.1, 1.0, 3.0
- Median	0.2	0.7	0.4
- Min, Max	0.2, 0.2	0.1, 3.0	0.1, 3.0
- 95% CI Mean	[.;.]	[0.2;1.6]	[0.2;1.5]
- 95% CI Median	[.;.]	[0.1;2.0]	[0.1;2.0]
Week 38: Study Eye - P			
- N	1	10	11
- Mean +/- SD	0.3 +/- .	0.7 +/- 0.9	0.6 +/-0.9
- p5, p25, p75, p95	0.3, 0.3, 0.3, 0.3	0.1, 0.1, 1.0, 3.0	0.1, 0.1, 1.0, 3.0
- Median	0.3	0.2	0.2
- Min, Max	0.3, 0.3	0.1, 3.0	0.1, 3.0
- 95% CI Mean	[.;.]	[0.0;1.3]	[0.0;1.2]
- 95% CI Median	[.;.]	[0.1;1.0]	[0.1;1.0]
Week 52: Study Eye - NO			
- N	3	11	14
- Mean +/- SD	1.6 +/- 1.3	2.1 +/- 1.3	2.0 +/-1.3
- p5, p25, p75, p95	0.4, 0.4, 3.0, 3.0	0.3, 1.0, 3.0, 4.0	0.3, 1.0, 3.0, 4.0
- Median	1.5	2.0	2.0
- Min, Max	0.4, 3.0	0.3, 4.0	0.3, 4.0
- 95% CI Mean	[-1.6;4.9]	[1.2;3.0]	[1.3;2.7]
- 95% CI Median	[0.4;3.0]	[1.0;4.0]	[1.0;3.0]
Week 52: Study Eye - NC			

	Treatment N=13	Control N=15	Total N=28
- N	3	11	14
- Mean +/- SD	1.6 +/- 1.4	2.4 +/- 1.5	2.2 +/-1.4
- p5, p25, p75, p95	0.3, 0.3, 3.0, 3.0	0.3, 1.0, 3.0, 5.0	0.3, 1.0, 3.0, 5.0
- Median	1.5	2.5	2.5
- Min, Max	0.3, 3.0	0.3, 5.0	0.3, 5.0
- 95% CI Mean	[-1.8;5.0]	[1.4;3.4]	[1.4;3.1]
- 95% CI Median	[0.3;3.0]	[1.0;4.0]	[1.0;3.0]
Week 52: Study Eye - C			
- N	3	11	14
- Mean +/- SD	1.6 +/- 1.2	1.8 +/- 1.3	1.8 +/-1.2
- p5, p25, p75, p95	0.2, 0.2, 2.5, 2.5	0.1, 1.0, 3.0, 4.0	0.1, 1.0, 3.0, 4.0
- Median	2.0	1.5	1.8
- Min, Max	0.2, 2.5	0.1, 4.0	0.1, 4.0
- 95% CI Mean	[-1.4;4.6]	[1.0;2.7]	[1.1;2.5]
- 95% CI Median	[0.2;2.5]	[1.0;3.0]	[1.0;3.0]
Week 52: Study Eye - P			
- N	3	11	14
- Mean +/- SD	0.8 +/- 1.0	1.0 +/- 0.9	1.0 +/-0.9
- p5, p25, p75, p95	0.1, 0.1, 2.0, 2.0	0.1, 0.2, 1.0, 3.0	0.1, 0.2, 1.0, 3.0
- Median	0.3	1.0	1.0
- Min, Max	0.1, 2.0	0.1, 3.0	0.1, 3.0
- 95% CI Mean	[-1.8;3.4]	[0.5;1.6]	[0.5;1.5]
- 95% CI Median	[0.1;2.0]	[0.2;2.0]	[0.2;2.0]
Week 104: Study Eye - NO			
- N	2	9	11
- Mean +/- SD	1.7 +/- 1.9	1.8 +/- 1.6	1.8 +/-1.5
- p5, p25, p75, p95	0.3, 0.3, 3.0, 3.0	0.1, 0.3, 3.0, 4.0	0.1, 0.3, 3.0, 4.0
- Median	1.7	2.0	2.0
- Min, Max	0.3, 3.0	0.1, 4.0	0.1, 4.0
- 95% CI Mean	[-15.5;18.8]	[0.6;3.0]	[0.8;2.8]
- 95% CI Median	[0.3;3.0]	[0.1;4.0]	[0.3;4.0]
Week 104: Study Eye - NC			
- N	2	9	11
- Mean +/- SD	1.7 +/- 1.9	2.0 +/- 1.7	2.0 +/-1.7
- p5, p25, p75, p95	0.3, 0.3, 3.0, 3.0	0.2, 0.3, 3.0, 5.0	0.2, 0.3, 3.0, 5.0
- Median	1.7	2.0	2.0
- Min, Max	0.3, 3.0	0.2, 5.0	0.2, 5.0
- 95% CI Mean	[-15.5;18.8]	[0.7;3.3]	[0.8;3.1]
- 95% CI Median	[0.3;3.0]	[0.2;4.0]	[0.3;4.0]
Week 104: Study Eye - C			
- N	2	9	11
- Mean +/- SD	1.1 +/- 1.3	1.7 +/- 1.6	1.6 +/-1.5
- p5, p25, p75, p95	0.2, 0.2, 2.0, 2.0	0.1, 0.3, 3.0, 4.0	0.1, 0.2, 3.0, 4.0
- Median	1.1	1.0	1.0
- Min, Max	0.2, 2.0	0.1, 4.0	0.1, 4.0
- 95% CI Mean	[-10.3;12.5]	[0.5;2.9]	[0.6;2.5]
- 95% CI Median	[0.2;2.0]	[0.2;3.0]	[0.2;3.0]
Week 104: Study Eye - P			
- N	2	9	11
- Mean +/- SD	1.2 +/- 1.2	0.7 +/- 0.6	0.8 +/-0.7
- p5, p25, p75, p95	0.3, 0.3, 2.0, 2.0	0.1, 0.2, 1.0, 2.0	0.1, 0.2, 1.0, 2.0
- Median	1.2	0.4	0.4
- Min, Max	0.3, 2.0	0.1, 2.0	0.1, 2.0
- 95% CI Mean	[-9.7;12.0]	[0.2;1.2]	[0.3;1.2]
- 95% CI Median	[0.3;2.0]	[0.1;1.0]	[0.2;2.0]

Table A 20: Fellow eye: Grading of cataract according to LOCS III (control examinations in week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Fellow Eye - NO			
- N	8	11	19
- Mean +/- SD	1.5 +/- 0.9	1.0 +/- 0.8	1.2 +/-0.9
- p5, p25, p75, p95	0.3, 1.0, 1.8, 3.5	0.2, 0.2, 1.5, 2.5	0.2, 0.3, 1.5, 3.5
- Median	1.5	0.4	1.5
- Min, Max	0.3, 3.5	0.2, 2.5	0.2, 3.5
- 95% CI Mean	[0.8;2.3]	[0.4;1.5]	[0.8;1.6]
- 95% CI Median	[1.0;3.5]	[0.2;2.0]	[0.4;1.5]
Week 12: Fellow Eye - NC			
- N	8	11	19
- Mean +/- SD	1.5 +/- 0.9	1.0 +/- 0.8	1.2 +/-0.9
- p5, p25, p75, p95	0.3, 1.0, 1.8, 3.5	0.2, 0.3, 1.5, 2.5	0.2, 0.3, 1.5, 3.5
- Median	1.5	0.4	1.5
- Min, Max	0.3, 3.5	0.2, 2.5	0.2, 3.5
- 95% CI Mean	[0.8;2.3]	[0.4;1.5]	[0.8;1.7]
- 95% CI Median	[1.0;3.5]	[0.3;2.0]	[0.4;1.5]
Week 12: Fellow Eye - C			
- N	8	11	19
- Mean +/- SD	1.0 +/- 1.2	1.0 +/- 1.1	1.0 +/-1.1
- p5, p25, p75, p95	0.0, 0.2, 1.5, 3.5	0.1, 0.1, 2.0, 3.0	0.0, 0.1, 2.0, 3.5
- Median	0.8	0.4	0.5
- Min, Max	0.0, 3.5	0.1, 3.0	0.0, 3.5
- 95% CI Mean	[0.0;2.0]	[0.2;1.7]	[0.5;1.5]
- 95% CI Median	[0.1;3.5]	[0.1;2.5]	[0.2;2.0]
Week 12: Fellow Eye - P			
- N	8	11	19
- Mean +/- SD	0.2 +/- 0.3	0.5 +/- 0.9	0.4 +/-0.7
- p5, p25, p75, p95	0.0, 0.1, 0.2, 1.0	0.1, 0.1, 0.2, 3.0	0.0, 0.1, 0.2, 3.0
- Median	0.1	0.1	0.1
- Min, Max	0.0, 1.0	0.1, 3.0	0.0, 3.0
- 95% CI Mean	[-0.1;0.5]	[-0.1;1.1]	[0.0;0.7]
- 95% CI Median	[0.1;1.0]	[0.1;1.0]	[0.1;0.2]
Week 26: Fellow Eye - NO			
- N	10	11	21
- Mean +/- SD	1.3 +/- 0.9	1.1 +/- 0.7	1.2 +/-0.8
- p5, p25, p75, p95	0.2, 0.3, 2.0, 3.0	0.2, 0.3, 1.5, 2.0	0.2, 0.3, 1.5, 2.0
- Median	1.5	1.5	1.5
- Min, Max	0.2, 3.0	0.2, 2.0	0.2, 3.0
- 95% CI Mean	[0.6;1.9]	[0.6;1.5]	[0.8;1.5]
- 95% CI Median	[0.3;2.0]	[0.3;2.0]	[0.3;1.5]
Week 26: Fellow Eye - NC			
- N	10	11	21
- Mean +/- SD	1.3 +/- 0.9	1.2 +/- 0.9	1.2 +/-0.9
- p5, p25, p75, p95	0.2, 0.3, 2.0, 3.0	0.3, 0.3, 1.5, 3.0	0.3, 0.3, 1.5, 3.0
- Median	1.5	1.5	1.5
- Min, Max	0.2, 3.0	0.3, 3.0	0.2, 3.0
- 95% CI Mean	[0.6;1.9]	[0.6;1.8]	[0.8;1.6]
- 95% CI Median	[0.3;2.0]	[0.3;2.0]	[0.3;1.5]
Week 26: Fellow Eye - C			
- N	10	11	21
- Mean +/- SD	0.6 +/- 0.9	0.8 +/- 0.8	0.7 +/-0.9
- p5, p25, p75, p95	0.0, 0.1, 1.0, 3.0	0.1, 0.1, 1.0, 2.5	0.1, 0.1, 1.0, 2.5
- Median	0.2	0.4	0.2
- Min, Max	0.0, 3.0	0.1, 2.5	0.0, 3.0
- 95% CI Mean	[-0.1;1.3]	[0.2;1.3]	[0.3;1.1]

	Treatment N=13	Control N=15	Total N=28
- 95% CI Median	[0.1;1.0]	[0.1;2.0]	[0.1;1.0]
Week 26: Fellow Eye - P			
- N	10	11	21
- Mean +/- SD	0.1 +/- 0.1	0.4 +/- 0.4	0.2 +/-0.3
- p5, p25, p75, p95	0.0, 0.1, 0.1, 0.3	0.1, 0.1, 1.0, 1.0	0.1, 0.1, 0.2, 1.0
- Median	0.1	0.1	0.1
- Min, Max	0.0, 0.3	0.1, 1.0	0.0, 1.0
- 95% CI Mean	[0.1;0.2]	[0.1;0.6]	[0.1;0.4]
- 95% CI Median	[0.1;0.2]	[0.1;1.0]	[0.1;0.2]
Week 38: Fellow Eye - NO			
- N	10	10	20
- Mean +/- SD	1.5 +/- 1.2	1.4 +/- 1.0	1.4 +/-1.1
- p5, p25, p75, p95	0.1, 0.3, 2.0, 4.0	0.3, 0.4, 2.0, 3.5	0.2, 0.4, 2.0, 3.8
- Median	1.5	1.0	1.3
- Min, Max	0.1, 4.0	0.3, 3.5	0.1, 4.0
- 95% CI Mean	[0.6;2.4]	[0.6;2.1]	[0.9;2.0]
- 95% CI Median	[0.3;3.0]	[0.4;2.0]	[0.4;2.0]
Week 38: Fellow Eye - NC			
- N	10	10	20
- Mean +/- SD	1.5 +/- 1.2	1.5 +/- 1.1	1.5 +/-1.2
- p5, p25, p75, p95	0.1, 0.3, 2.0, 4.0	0.3, 0.4, 2.0, 3.5	0.2, 0.4, 2.0, 3.8
- Median	1.5	1.0	1.3
- Min, Max	0.1, 4.0	0.3, 3.5	0.1, 4.0
- 95% CI Mean	[0.6;2.4]	[0.7;2.3]	[1.0;2.0]
- 95% CI Median	[0.3;3.0]	[0.4;3.0]	[0.4;2.0]
Week 38: Fellow Eye - C			
- N	10	10	20
- Mean +/- SD	1.0 +/- 1.4	0.9 +/- 1.1	1.0 +/-1.2
- p5, p25, p75, p95	0.0, 0.1, 1.5, 4.0	0.1, 0.1, 1.0, 3.5	0.1, 0.1, 1.3, 3.8
- Median	0.2	0.7	0.3
- Min, Max	0.0, 4.0	0.1, 3.5	0.0, 4.0
- 95% CI Mean	[-0.0;2.0]	[0.2;1.7]	[0.4;1.6]
- 95% CI Median	[0.1;3.0]	[0.1;2.0]	[0.1;1.0]
Week 38: Fellow Eye - P			
- N	10	10	20
- Mean +/- SD	0.5 +/- 1.2	1.0 +/- 1.5	0.7 +/-1.3
- p5, p25, p75, p95	0.0, 0.1, 0.1, 4.0	0.1, 0.1, 1.0, 5.0	0.1, 0.1, 1.0, 4.5
- Median	0.1	0.6	0.1
- Min, Max	0.0, 4.0	0.1, 5.0	0.0, 5.0
- 95% CI Mean	[-0.4;1.4]	[-0.1;2.0]	[0.1;1.4]
- 95% CI Median	[0.1;0.3]	[0.1;1.0]	[0.1;1.0]
Week 52: Fellow Eye - NO			
- N	8	13	21
- Mean +/- SD	1.5 +/- 1.1	1.8 +/- 1.4	1.7 +/-1.3
- p5, p25, p75, p95	0.2, 0.7, 2.3, 3.0	0.2, 0.4, 3.0, 4.0	0.2, 0.4, 3.0, 4.0
- Median	1.5	2.0	1.5
- Min, Max	0.2, 3.0	0.2, 4.0	0.2, 4.0
- 95% CI Mean	[0.6;2.4]	[0.9;2.6]	[1.1;2.2]
- 95% CI Median	[0.3;3.0]	[0.3;3.0]	[0.4;3.0]
Week 52: Fellow Eye - NC			
- N	8	13	21
- Mean +/- SD	1.5 +/- 1.1	2.1 +/- 1.3	1.9 +/-1.2
- p5, p25, p75, p95	0.2, 0.7, 2.3, 3.0	0.3, 1.0, 3.0, 4.0	0.3, 1.0, 3.0, 4.0
- Median	1.5	2.0	1.5
- Min, Max	0.2, 3.0	0.3, 4.0	0.2, 4.0
- 95% CI Mean	[0.6;2.4]	[1.3;2.9]	[1.3;2.4]

	Treatment N=13	Control N=15	Total N=28
- 95% CI Median	[0.3;3.0]	[0.4;3.0]	[1.0;3.0]
Week 52: Fellow Eye - C			
- N	8	13	21
- Mean +/- SD	1.0 +/- 1.2	1.5 +/- 1.3	1.3 +/-1.2
- p5, p25, p75, p95	0.0, 0.1, 1.5, 3.5	0.1, 0.4, 2.0, 4.0	0.1, 0.2, 2.0, 3.5
- Median	0.6	1.0	1.0
- Min, Max	0.0, 3.5	0.1, 4.0	0.0, 4.0
- 95% CI Mean	[-0.0;2.0]	[0.7;2.2]	[0.7;1.8]
- 95% CI Median	[0.1;3.5]	[0.2;3.0]	[0.2;2.0]
Week 52: Fellow Eye - P			
- N	8	13	21
- Mean +/- SD	0.6 +/- 0.9	0.7 +/- 0.6	0.7 +/-0.7
- p5, p25, p75, p95	0.0, 0.1, 1.2, 2.0	0.1, 0.2, 1.0, 2.0	0.1, 0.1, 1.0, 2.0
- Median	0.1	1.0	0.3
- Min, Max	0.0, 2.0	0.1, 2.0	0.0, 2.0
- 95% CI Mean	[-0.1;1.3]	[0.4;1.0]	[0.3;1.0]
- 95% CI Median	[0.1;2.0]	[0.1;1.0]	[0.1;1.0]
Week 104: Fellow Eye - NO			
- N	10	11	21
- Mean +/- SD	1.1 +/- 1.0	1.6 +/- 1.5	1.4 +/-1.3
- p5, p25, p75, p95	0.2, 0.3, 1.5, 3.0	0.2, 0.3, 3.0, 4.0	0.2, 0.3, 2.0, 4.0
- Median	0.8	1.0	1.0
- Min, Max	0.2, 3.0	0.2, 4.0	0.2, 4.0
- 95% CI Mean	[0.4;1.8]	[0.6;2.6]	[0.8;1.9]
- 95% CI Median	[0.3;2.5]	[0.3;4.0]	[0.3;2.0]
Week 104: Fellow Eye - NC			
- N	10	11	21
- Mean +/- SD	1.2 +/- 1.0	1.8 +/- 1.4	1.5 +/-1.2
- p5, p25, p75, p95	0.2, 0.3, 1.5, 3.0	0.3, 0.6, 3.0, 4.0	0.3, 0.6, 2.0, 4.0
- Median	0.8	1.5	1.5
- Min, Max	0.2, 3.0	0.3, 4.0	0.2, 4.0
- 95% CI Mean	[0.5;1.8]	[0.9;2.7]	[0.9;2.0]
- 95% CI Median	[0.3;2.5]	[0.6;4.0]	[0.6;2.0]
Week 104: Fellow Eye - C			
- N	10	11	21
- Mean +/- SD	0.4 +/- 0.6	1.4 +/- 1.3	1.0 +/-1.2
- p5, p25, p75, p95	0.1, 0.1, 0.7, 2.0	0.1, 0.2, 3.0, 4.0	0.1, 0.1, 1.0, 3.0
- Median	0.1	1.0	0.7
- Min, Max	0.1, 2.0	0.1, 4.0	0.1, 4.0
- 95% CI Mean	[-0.0;0.9]	[0.5;2.3]	[0.4;1.5]
- 95% CI Median	[0.1;0.7]	[0.2;3.0]	[0.1;1.0]
Week 104: Fellow Eye - P			
- N	10	11	21
- Mean +/- SD	0.5 +/- 0.6	0.6 +/- 0.6	0.6 +/-0.6
- p5, p25, p75, p95	0.1, 0.1, 0.8, 2.0	0.1, 0.1, 1.0, 2.0	0.1, 0.1, 0.8, 2.0
- Median	0.1	0.8	0.2
- Min, Max	0.1, 2.0	0.1, 2.0	0.1, 2.0
- 95% CI Mean	[0.0;0.9]	[0.3;1.0]	[0.3;0.8]
- 95% CI Median	[0.1;1.0]	[0.1;1.0]	[0.1;0.8]

Table A 21 shows the results of the examination of differential light sensitivity in the visual field (Goldman perimetry). The visual field was recorded in the study eye using the standardized Goldmann apparatus. As test spot the III4 spot was used. Only the outer edges of the visual field were examined and added to the

CRF. The outer edges of the visual field were documented along eight main meridians in degrees: superior (s), superior-nasal(sn), nasal (n), inferior-nasal (in), inferior (i), inferior-temporal (it), temporal (t), and temporal-superior (ts).

Table A 21: Study eye: Goldman Perimetry (control examinations in week 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 52: Goldman perimetry - Superior temporal margin			
- N	10	13	23
- Mean +/- SD	35.4 +/- 18.4	32.4 +/- 23.6	33.7 +/-21.1
- p5, p25, p75, p95	0.0, 21.0, 52.0, 58.0	4.0, 6.0, 44.0, 70.0	4.0, 17.0, 52.0, 69.0
- Median	35.5	35.0	35.0
- Min, Max	0.0, 58.0	4.0, 70.0	0.0, 70.0
- 95% CI Mean	[22.2;48.6]	[18.2;46.7]	[24.6;42.8]
- 95% CI Median	[17.0;55.0]	[5.8;58.0]	[21.0;45.0]
Week 52: Goldman perimetry - Superior margin			
- N	10	13	23
- Mean +/- SD	29.0 +/- 14.6	35.4 +/- 11.9	32.6 +/-13.2
- p5, p25, p75, p95	0.0, 15.0, 42.0, 45.0	20.0, 28.0, 40.0, 56.0	15.0, 24.0, 42.0, 52.0
- Median	32.0	36.0	32.0
- Min, Max	0.0, 45.0	20.0, 56.0	0.0, 56.0
- 95% CI Mean	[18.6;39.4]	[28.2;42.6]	[26.9;38.3]
- 95% CI Median	[15.0;42.0]	[24.0;50.0]	[28.0;40.0]
Week 52: Goldman perimetry - Superior nasal margin			
- N	10	13	23
- Mean +/- SD	33.0 +/- 16.0	39.8 +/- 9.6	36.8 +/-12.9
- p5, p25, p75, p95	0.0, 23.0, 45.0, 52.0	25.0, 35.0, 42.0, 58.0	15.0, 31.0, 45.0, 55.0
- Median	39.0	36.0	38.0
- Min, Max	0.0, 52.0	25.0, 58.0	0.0, 58.0
- 95% CI Mean	[21.5;44.5]	[34.0;45.6]	[31.2;42.4]
- 95% CI Median	[15.0;46.0]	[34.0;50.0]	[34.0;42.0]
Week 52: Goldman perimetry - Temporal margin			
- N	10	13	23
- Mean +/- SD	42.7 +/- 15.0	57.8 +/- 16.2	51.3 +/-17.2
- p5, p25, p75, p95	24.0, 29.0, 55.0, 62.0	16.0, 55.0, 68.0, 75.0	24.0, 37.0, 65.0, 71.0
- Median	43.5	63.0	55.0
- Min, Max	24.0, 62.0	16.0, 75.0	16.0, 75.0
- 95% CI Mean	[32.0;53.4]	[48.1;67.6]	[43.8;58.7]
- 95% CI Median	[24.0;59.0]	[48.0;70.0]	[37.0;63.0]
Week 52: Goldman perimetry - Nasal margin			
- N	10	13	23
- Mean +/- SD	34.8 +/- 12.9	47.5 +/- 9.8	42.0 +/-12.7
- p5, p25, p75, p95	14.0, 28.0, 46.0, 51.0	32.0, 40.0, 55.0, 62.0	15.0, 35.0, 51.0, 61.0
- Median	36.0	45.0	44.0
- Min, Max	14.0, 51.0	32.0, 62.0	14.0, 62.0
- 95% CI Mean	[25.5;44.1]	[41.5;53.4]	[36.4;47.5]
- 95% CI Median	[15.0;50.0]	[40.0;60.0]	[35.0;50.0]
Week 52: Goldman perimetry - Inferior temporal margin			
- N	10	13	23
- Mean +/- SD	41.5 +/- 16.4	59.9 +/- 19.0	51.9 +/-19.8
- p5, p25, p75, p95	18.0, 28.0, 52.0, 72.0	15.0, 58.0, 72.0, 85.0	18.0, 40.0, 70.0, 78.0
- Median	42.5	63.0	53.0

	Treatment N=13	Control N=15	Total N=28
- Min, Max	18.0, 72.0	15.0, 85.0	15.0, 85.0
- 95% CI Mean	[29.8;53.2]	[48.5;71.4]	[43.3;60.5]
- 95% CI Median	[20.0;53.0]	[43.0;74.0]	[40.0;65.0]
Week 52: Goldman perimetry - Inferior margin			
- N	10	13	23
- Mean +/- SD	36.8 +/- 14.5	50.4 +/- 13.5	44.5 +/-15.3
- p5, p25, p75, p95	13.0, 21.0, 50.0, 53.0	27.0, 40.0, 61.0, 62.0	21.0, 30.0, 60.0, 62.0
- Median	41.5	58.0	50.0
- Min, Max	13.0, 53.0	27.0, 62.0	13.0, 62.0
- 95% CI Mean	[26.4;47.2]	[42.2;58.5]	[37.9;51.1]
- 95% CI Median	[21.0;52.0]	[32.0;62.0]	[32.0;58.0]
Week 52: Goldman perimetry - Inferior nasal margin			
- N	9	13	22
- Mean +/- SD	34.8 +/- 12.4	44.8 +/- 9.6	40.7 +/-11.7
- p5, p25, p75, p95	13.0, 31.0, 42.0, 45.0	29.0, 43.0, 47.0, 70.0	15.0, 41.0, 46.0, 48.0
- Median	41.0	45.0	43.0
- Min, Max	13.0, 45.0	29.0, 70.0	13.0, 70.0
- 95% CI Mean	[25.2;44.3]	[39.1;50.6]	[35.5;45.9]
- 95% CI Median	[15.0;43.0]	[41.0;48.0]	[41.0;46.0]
Week 104: Goldman perimetry - Superior temporal margin			
- N	11	13	24
- Mean +/- SD	38.5 +/- 18.8	35.8 +/- 22.2	37.0 +/-20.3
- p5, p25, p75, p95	4.5, 30.0, 52.0, 58.0	3.0, 18.0, 58.0, 63.0	4.5, 20.0, 54.5, 60.0
- Median	40.0	42.0	41.5
- Min, Max	4.5, 58.0	3.0, 63.0	3.0, 63.0
- 95% CI Mean	[25.8;51.2]	[22.4;49.2]	[28.5;45.6]
- 95% CI Median	[30.0;57.0]	[6.5;58.0]	[30.0;52.0]
Week 104: Goldman perimetry - Superior margin			
- N	11	13	24
- Mean +/- SD	37.0 +/- 11.3	37.4 +/- 10.8	37.2 +/-10.8
- p5, p25, p75, p95	10.0, 30.0, 45.0, 51.0	20.0, 30.0, 48.0, 55.0	20.0, 30.0, 46.5, 52.0
- Median	38.0	32.0	38.0
- Min, Max	10.0, 51.0	20.0, 55.0	10.0, 55.0
- 95% CI Mean	[29.4;44.6]	[30.8;43.9]	[32.6;41.8]
- 95% CI Median	[30.0;50.0]	[30.0;50.0]	[32.0;45.0]
Week 104: Goldman perimetry - Superior nasal margin			
- N	11	13	24
- Mean +/- SD	41.6 +/- 17.2	39.8 +/- 13.4	40.7 +/-14.9
- p5, p25, p75, p95	10.0, 30.0, 52.0, 68.0	18.0, 30.0, 48.0, 60.0	18.0, 30.0, 50.0, 65.0
- Median	42.0	45.0	43.0
- Min, Max	10.0, 68.0	18.0, 60.0	10.0, 68.0
- 95% CI Mean	[30.1;53.2]	[31.8;47.9]	[34.4;47.0]
- 95% CI Median	[30.0;65.0]	[30.0;52.0]	[30.0;48.0]
Week 104: Goldman perimetry - Temporal margin			
- N	11	13	24
- Mean +/- SD	49.0 +/- 8.5	55.4 +/- 19.6	52.5 +/-15.5
- p5, p25, p75, p95	30.0, 45.0, 57.0, 58.0	16.0, 48.0, 70.0, 76.0	20.0, 45.0, 62.5, 75.0
- Median	50.0	60.0	55.0
- Min, Max	30.0, 58.0	16.0, 76.0	16.0, 76.0
- 95% CI Mean	[43.3;54.7]	[43.6;67.2]	[45.9;59.0]
- 95% CI Median	[45.0;58.0]	[40.0;71.0]	[48.0;60.0]

	Treatment N=13	Control N=15	Total N=28
Week 104: Goldman perimetry - Nasal margin			
- N	11	13	24
- Mean +/- SD	42.5 +/- 16.1	42.7 +/- 15.1	42.6 +/-15.2
- p5, p25, p75, p95	20.0, 32.0, 46.0, 80.0	18.0, 30.0, 57.0, 62.0	20.0, 31.0, 53.5, 62.0
- Median	42.0	45.0	42.0
- Min, Max	20.0, 80.0	18.0, 62.0	18.0, 80.0
- 95% CI Mean	[31.6;53.3]	[33.6;51.8]	[36.2;49.0]
- 95% CI Median	[32.0;58.0]	[30.0;59.0]	[32.0;50.0]
Week 104: Goldman perimetry - Inferior temporal margin			
- N	11	13	24
- Mean +/- SD	47.4 +/- 14.0	54.6 +/- 19.8	51.3 +/-17.4
- p5, p25, p75, p95	20.0, 38.0, 55.0, 74.0	20.0, 46.0, 70.0, 80.0	20.0, 40.5, 60.0, 80.0
- Median	51.0	59.0	54.5
- Min, Max	20.0, 74.0	20.0, 80.0	20.0, 80.0
- 95% CI Mean	[37.9;56.8]	[42.7;66.6]	[43.9;58.6]
- 95% CI Median	[38.0;55.0]	[35.0;70.0]	[46.0;60.0]
Week 104: Goldman perimetry - Inferior margin			
- N	11	13	24
- Mean +/- SD	43.2 +/- 12.2	47.3 +/- 15.5	45.4 +/-13.9
- p5, p25, p75, p95	20.0, 31.0, 54.0, 55.0	15.0, 43.0, 55.0, 72.0	20.0, 37.0, 54.0, 62.0
- Median	50.0	50.0	50.0
- Min, Max	20.0, 55.0	15.0, 72.0	15.0, 72.0
- 95% CI Mean	[35.0;51.4]	[38.0;56.7]	[39.5;51.3]
- 95% CI Median	[31.0;54.0]	[40.0;61.0]	[43.0;54.0]
Week 104: Goldman perimetry - Inferior nasal margin			
- N	11	13	24
- Mean +/- SD	42.7 +/- 14.0	41.3 +/- 13.7	42.0 +/-13.6
- p5, p25, p75, p95	25.0, 30.0, 51.0, 65.0	15.0, 38.0, 48.0, 68.0	20.0, 32.0, 50.0, 65.0
- Median	45.0	41.0	43.0
- Min, Max	25.0, 65.0	15.0, 68.0	15.0, 68.0
- 95% CI Mean	[33.3;52.1]	[33.0;49.6]	[36.2;47.7]
- 95% CI Median	[30.0;64.0]	[34.0;50.0]	[34.0;50.0]

Table A 22 shows the results from the slitlamp examination. The assessments of the anterior segment (external eye, cornea, anterior chamber, lens) and the assessment of the posterior segment (vitreous cavity, retinal attachment, retinal abnormalities, foveal position, recurrence) is presented.

Table A 22: Study eye: slitlamp examination (control examinations in week 12, 26, 38, 52 and 104).

	Treatment N=13	Control N=15	Total N=28
Week 12: External eye			
- Normal	6 (75.0%)	11 (91.7%)	17 (85.0%)
- Other	1 (12.5%)	1 (8.3%)	2 (10.0%)
- Mod. inflamm.+Other	1 (12.5%)	0 (0.0%)	1 (5.0%)
- missing	5	2	7
Week 12: Cornea			
- Normal	7 (87.5%)	12 (100.0%)	19 (95.0%)
- Dry Eye	1 (12.5%)	0 (0.0%)	1 (5.0%)
- missing	5	2	7
Week 12: Anterior chamber			

	Treatment N=13	Control N=15	Total N=28
- Normal	8 (100.0%)	12 (100.0%)	20 (100.0%)
- missing	5	2	7
Week 12: Lens			
- Normal	2 (25.0%)	7 (58.3%)	9 (45.0%)
- Posterior cataract	0 (0.0%)	2 (16.7%)	2 (10.0%)
- Pseudophakic	5 (62.5%)	0 (0.0%)	5 (25.0%)
- Other	1 (12.5%)	2 (16.7%)	3 (15.0%)
- Pseudophakic+Other	0 (0.0%)	1 (8.3%)	1 (5.0%)
- missing	5	2	7
Week 12: Vitreous cavity			
- Normal	7 (87.5%)	9 (75.0%)	16 (80.0%)
- Cloudy	0 (0.0%)	1 (8.3%)	1 (5.0%)
- Other	1 (12.5%)	1 (8.3%)	2 (10.0%)
- Normal + Other	0 (0.0%)	1 (8.3%)	1 (5.0%)
- missing	5	2	7
Week 12: Retinal attachment			
- Completely attached	7 (87.5%)	11 (91.7%)	18 (90.0%)
- Other	0 (0.0%)	1 (8.3%)	1 (5.0%)
- Compl. attached + Other	1 (12.5%)	0 (0.0%)	1 (5.0%)
- missing	5	2	7
Week 12: Retinal abnormalities			
- Pucker	0 (0.0%)	2 (16.7%)	2 (10.0%)
- Subret.hemorrhage	0 (0.0%)	2 (16.7%)	2 (10.0%)
- No abnorm.	6 (75.0%)	3 (25.0%)	9 (45.0%)
- Other	2 (25.0%)	4 (33.3%)	6 (30.0%)
- Edema & Subretinal hemorrhage	0 (0.0%)	1 (8.3%)	1 (5.0%)
- missing	5	2	7
Week 12: Foveal position			
- Outside the defect area	8 (100.0%)	0 (0.0%)	8 (42.1%)
- Within the defect area	0 (0.0%)	11 (100.0%)	11 (57.9%)
- missing	5	2	7
Week 12: Recurrence			
- no	8 (100.0%)	10 (100.0%)	18 (100.0%)
- missing	5	4	9
Week 26: External eye			
- Normal	12 (100.0%)	12 (100.0%)	24 (100.0%)
- missing	1	2	3
Week 26: Cornea			
- Normal	10 (83.3%)	11 (91.7%)	21 (87.5%)
- Dry Eye	0 (0.0%)	1 (8.3%)	1 (4.2%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.2%)
- Normal + Other	1 (8.3%)	0 (0.0%)	1 (4.2%)
- missing	1	2	3
Week 26: Anterior chamber			
- Normal	10 (83.3%)	12 (100.0%)	22 (91.7%)
- Other	2 (16.7%)	0 (0.0%)	2 (8.3%)
- missing	1	2	3
Week 26: Lens			
- Normal	4 (33.3%)	6 (50.0%)	10 (41.7%)
- Posterior cataract	1 (8.3%)	3 (25.0%)	4 (16.7%)
- Pseudophakic	5 (41.7%)	0 (0.0%)	5 (20.8%)
- Other	0 (0.0%)	2 (16.7%)	2 (8.3%)
- Pseudophakic+Other	2 (16.7%)	1 (8.3%)	3 (12.5%)

	Treatment N=13	Control N=15	Total N=28
- missing	1	2	3
Week 26: Vitreous cavity			
- Normal	10 (83.3%)	10 (83.3%)	20 (83.3%)
- Cloudy	1 (8.3%)	1 (8.3%)	2 (8.3%)
- Silicone filled	1 (8.3%)	0 (0.0%)	1 (4.2%)
- Normal + Other	0 (0.0%)	1 (8.3%)	1 (4.2%)
- missing	1	2	3
Week 26: Retinal attachment			
- Completely attached	11 (91.7%)	12 (100.0%)	23 (95.8%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.2%)
- missing	1	2	3
Week 26: Retinal abnormalities			
- Pucker	1 (8.3%)	0 (0.0%)	1 (4.2%)
- Edema	1 (8.3%)	0 (0.0%)	1 (4.2%)
- Subret.hemorrhage	0 (0.0%)	1 (8.3%)	1 (4.2%)
- Subret.fibrosis	2 (16.7%)	1 (8.3%)	3 (12.5%)
- No abnorm.	5 (41.7%)	4 (33.3%)	9 (37.5%)
- Other	3 (25.0%)	3 (25.0%)	6 (25.0%)
- Subretinal hemorrhage & Subretinal fibrosis	0 (0.0%)	2 (16.7%)	2 (8.3%)
- Subretinal hemorrhage & other	0 (0.0%)	1 (8.3%)	1 (4.2%)
- missing	1	2	3
Week 26: Foveal position			
- Outside the defect area	10 (83.3%)	0 (0.0%)	10 (45.5%)
- Within the defect area	2 (16.7%)	10 (100.0%)	12 (54.5%)
- missing	1	3	4
Week 26: Recurrence			
- no	12 (100.0%)	10 (100.0%)	22 (100.0%)
- missing	1	4	5
Week 38: External eye			
- Normal	11 (91.7%)	11 (100.0%)	22 (95.7%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.3%)
- missing	1	3	4
Week 38: Cornea			
- Normal	10 (83.3%)	11 (100.0%)	21 (91.3%)
- Dry Eye	1 (8.3%)	0 (0.0%)	1 (4.3%)
- Dry Eye + Other	1 (8.3%)	0 (0.0%)	1 (4.3%)
- missing	1	3	4
Week 38: Anterior chamber			
- Normal	11 (91.7%)	11 (100.0%)	22 (95.7%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.3%)
- missing	1	3	4
Week 38: Lens			
- Normal	4 (33.3%)	7 (63.6%)	11 (47.8%)
- Posterior cataract	0 (0.0%)	2 (18.2%)	2 (8.7%)
- Pseudophakic	4 (33.3%)	1 (9.1%)	5 (21.7%)
- Other	2 (16.7%)	1 (9.1%)	3 (13.0%)
- Pseudophakic+Other	2 (16.7%)	0 (0.0%)	2 (8.7%)
- missing	1	3	4
Week 38: Vitreous cavity			
- Normal	7 (58.3%)	10 (90.9%)	17 (73.9%)
- Cloudy	2 (16.7%)	1 (9.1%)	3 (13.0%)
- Silicone filled	3 (25.0%)	0 (0.0%)	3 (13.0%)
- missing	1	3	4

	Treatment N=13	Control N=15	Total N=28
Week 38: Retinal attachment			
- Completely attached	12 (100.0%)	11 (100.0%)	23 (100.0%)
- missing	1	3	4
Week 38: Retinal abnormalities			
- Pucker	1 (8.3%)	0 (0.0%)	1 (4.3%)
- Edema	1 (8.3%)	2 (18.2%)	3 (13.0%)
- Subret.fibrosis	0 (0.0%)	2 (18.2%)	2 (8.7%)
- PVR	1 (8.3%)	0 (0.0%)	1 (4.3%)
- No abnorm.	4 (33.3%)	1 (9.1%)	5 (21.7%)
- Other	2 (16.7%)	3 (27.3%)	5 (21.7%)
- Edema & Subretinal hemorrhage	1 (8.3%)	0 (0.0%)	1 (4.3%)
- Edema & Subretinal fibrosis	1 (8.3%)	0 (0.0%)	1 (4.3%)
- Subretinal hemorrhage & Subretinal fibrosis	0 (0.0%)	2 (18.2%)	2 (8.7%)
- Subretinal fibrosis & other	0 (0.0%)	1 (9.1%)	1 (4.3%)
- Pucker & Subretinal hemorrhage & other	1 (8.3%)	0 (0.0%)	1 (4.3%)
- missing	1	3	4
Week 38: Foveal position			
- Outside the defect area	10 (83.3%)	0 (0.0%)	10 (43.5%)
- Within the defect area	2 (16.7%)	11 (100.0%)	13 (56.5%)
- missing	1	3	4
Week 38: Recurrence			
- no	12 (100.0%)	9 (100.0%)	21 (100.0%)
- missing	1	5	6
Week 52: External eye			
- Normal	12 (100.0%)	14 (100.0%)	26 (100.0%)
- missing	1	0	1
Week 52: Cornea			
- Normal	9 (75.0%)	12 (85.7%)	21 (80.8%)
- Dry Eye	1 (8.3%)	1 (7.1%)	2 (7.7%)
- Other	1 (8.3%)	0 (0.0%)	1 (3.8%)
- Normal + Other	1 (8.3%)	0 (0.0%)	1 (3.8%)
- Erosio + Other	0 (0.0%)	1 (7.1%)	1 (3.8%)
- missing	1	0	1
Week 52: Anterior chamber			
- Normal	9 (75.0%)	14 (100.0%)	23 (88.5%)
- Moderate Inflammation	1 (8.3%)	0 (0.0%)	1 (3.8%)
- Other	2 (16.7%)	0 (0.0%)	2 (7.7%)
- missing	1	0	1
Week 52: Lens			
- Normal	3 (25.0%)	5 (35.7%)	8 (30.8%)
- Posterior cataract	2 (16.7%)	5 (35.7%)	7 (26.9%)
- Pseudophakic	5 (41.7%)	2 (14.3%)	7 (26.9%)
- Other	0 (0.0%)	1 (7.1%)	1 (3.8%)
- Pseudophakic+Other	2 (16.7%)	1 (7.1%)	3 (11.5%)
- missing	1	0	1
Week 52: Vitreous cavity			
- Normal	10 (83.3%)	12 (85.7%)	22 (84.6%)
- Cloudy	1 (8.3%)	1 (7.1%)	2 (7.7%)
- Silicone filled	1 (8.3%)	0 (0.0%)	1 (3.8%)
- Other	0 (0.0%)	1 (7.1%)	1 (3.8%)
- missing	1	0	1
Week 52: Retinal attachment			

	Treatment N=13	Control N=15	Total N=28
- Completely attached	12 (100.0%)	12 (92.3%)	24 (96.0%)
- Other	0 (0.0%)	1 (7.7%)	1 (4.0%)
- missing	1	0	1
Week 52: Retinal abnormalities			
- Edema	1 (8.3%)	0 (0.0%)	1 (4.0%)
- Subret.hemorrhage	0 (0.0%)	1 (7.7%)	1 (4.0%)
- Subret.fibrosis	2 (16.7%)	4 (30.8%)	6 (24.0%)
- No abnorm.	4 (33.3%)	1 (7.7%)	5 (20.0%)
- Other	5 (41.7%)	4 (30.8%)	9 (36.0%)
- Subretinal hemorrhage & Subretinal fibrosis	0 (0.0%)	1 (7.7%)	1 (4.0%)
- Subretinal fibrosis & other	0 (0.0%)	2 (15.4%)	2 (8.0%)
- missing	1	1	2
Week 52: Foveal position			
- Outside the defect area	8 (72.7%)	1 (7.7%)	9 (37.5%)
- Adjacent to the defect	1 (9.1%)	0 (0.0%)	1 (4.2%)
- Within the defect area	2 (18.2%)	12 (92.3%)	14 (58.3%)
- missing	2	0	2
Week 52: Recurrence			
- no	11 (91.7%)	12 (100.0%)	23 (95.8%)
- yes	1 (8.3%)	0 (0.0%)	1 (4.2%)
- missing	1	2	3
Week 104: External eye			
- Normal	10 (83.3%)	13 (100.0%)	23 (92.0%)
- Other	2 (16.7%)	0 (0.0%)	2 (8.0%)
- missing	1	1	2
Week 104: Cornea			
- Normal	8 (66.7%)	12 (92.3%)	20 (80.0%)
- Dry Eye	2 (16.7%)	1 (7.7%)	3 (12.0%)
- Other	2 (16.7%)	0 (0.0%)	2 (8.0%)
- missing	1	1	2
Week 104: Anterior chamber			
- Normal	11 (91.7%)	13 (100.0%)	24 (96.0%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.0%)
- missing	1	1	2
Week 104: Lens			
- Normal	2 (16.7%)	8 (61.5%)	10 (40.0%)
- Posterior cataract	1 (8.3%)	3 (23.1%)	4 (16.0%)
- Pseudophakic	8 (66.7%)	2 (15.4%)	10 (40.0%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.0%)
- missing	1	1	2
Week 104: Vitreous cavity			
- Normal	8 (66.7%)	13 (100.0%)	21 (84.0%)
- Cloudy	2 (16.7%)	0 (0.0%)	2 (8.0%)
- Silicone filled	2 (16.7%)	0 (0.0%)	2 (8.0%)
- missing	1	1	2
Week 104: Retinal attachment			
- Completely attached	10 (83.3%)	13 (100.0%)	23 (92.0%)
- Other	1 (8.3%)	0 (0.0%)	1 (4.0%)
- Compl. attached + Other	1 (8.3%)	0 (0.0%)	1 (4.0%)
- missing	1	1	2
Week 104: Retinal abnormalities			
- Pucker	2 (16.7%)	1 (8.3%)	3 (12.5%)
- Edema	1 (8.3%)	0 (0.0%)	1 (4.2%)

	Treatment N=13	Control N=15	Total N=28
- Subret.fibrosis	1 (8.3%)	1 (8.3%)	2 (8.3%)
- No abnorm.	5 (41.7%)	2 (16.7%)	7 (29.2%)
- Other	2 (16.7%)	2 (16.7%)	4 (16.7%)
- Edema & other	0 (0.0%)	1 (8.3%)	1 (4.2%)
- Subretinal hemorrhage & other	0 (0.0%)	1 (8.3%)	1 (4.2%)
- Subretinal fibrosis & other	1 (8.3%)	4 (33.3%)	5 (20.8%)
- missing	1	2	3
Week 104: Foveal position			
- Outside the defect area	10 (83.3%)	1 (7.7%)	11 (44.0%)
- Within the defect area	2 (16.7%)	12 (92.3%)	14 (56.0%)
- missing	1	1	2
Week 104: Recurrence			
- no	12 (100.0%)	11 (100.0%)	23 (100.0%)
- missing	1	1	2

Table A 23 summarizes the results from measuring the intraocular pressure (tonometry) in the study eye.

Table A 23: Study eye: Tonometry (week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12			
- N	8	12	20
- Mean +/- SD	10.5 +/- 3.2	12.8 +/- 2.1	11.9 +/-2.7
- p5, p25, p75, p95	6.0, 8.5, 13.0, 15.0	9.0, 12.0, 14.0, 15.0	7.0, 9.5, 14.0, 15.0
- Median	10.0	13.0	13.0
- Min, Max	6.0, 15.0	9.0, 15.0	6.0, 15.0
- 95% CI Mean	[7.9;13.1]	[11.4;14.1]	[10.6;13.1]
- 95% CI Median	[8.0;15.0]	[11.0;14.0]	[10.0;14.0]
Week 26			
- N	12	12	24
- Mean +/- SD	11.3 +/- 6.6	14.6 +/- 3.3	12.9 +/-5.3
- p5, p25, p75, p95	4.0, 5.0, 17.5, 21.0	11.0, 12.5, 15.5, 21.0	4.0, 10.5, 16.5, 21.0
- Median	10.5	13.5	13.0
- Min, Max	4.0, 21.0	11.0, 21.0	4.0, 21.0
- 95% CI Mean	[7.1;15.4]	[12.5;16.7]	[10.7;15.2]
- 95% CI Median	[5.0;18.0]	[12.0;16.0]	[11.0;16.0]
Week 38			
- N	12	11	23
- Mean +/- SD	12.1 +/- 6.6	13.4 +/- 2.6	12.7 +/-5.0
- p5, p25, p75, p95	1.0, 7.5, 17.0, 24.0	10.0, 12.0, 14.0, 19.0	3.0, 11.0, 17.0, 19.0
- Median	12.5	13.0	13.0
- Min, Max	1.0, 24.0	10.0, 19.0	1.0, 24.0
- 95% CI Mean	[7.9;16.3]	[11.6;15.1]	[10.5;14.9]
- 95% CI Median	[7.0;17.0]	[12.0;17.0]	[12.0;14.0]
Week 52			
- N	12	14	26
- Mean +/- SD	12.8 +/- 5.8	13.5 +/- 2.1	13.2 +/-4.1
- p5, p25, p75, p95	4.0, 9.5, 16.0, 22.0	10.0, 12.0, 14.0, 18.0	5.0, 11.0, 15.0, 22.0
- Median	11.5	14.0	13.5
- Min, Max	4.0, 22.0	10.0, 18.0	4.0, 22.0
- 95% CI Mean	[9.1;16.4]	[12.3;14.7]	[11.5;14.8]
- 95% CI Median	[8.0;17.0]	[12.0;15.0]	[11.0;15.0]
Week 104			
- N	12	13	25
- Mean +/- SD	12.7 +/- 5.9	14.8 +/- 1.9	13.8 +/-4.4
- p5, p25, p75, p95	2.0, 8.5, 16.0, 23.0	12.0, 14.0, 16.0, 19.0	5.0, 13.0, 16.0, 19.0
- Median	13.5	14.0	14.0
- Min, Max	2.0, 23.0	12.0, 19.0	2.0, 23.0
- 95% CI Mean	[8.9;16.4]	[13.6;15.9]	[12.0;15.6]
- 95% CI Median	[7.0;17.0]	[13.0;16.0]	[13.0;15.0]

Table A 24 shows the assessment of cyclorotation (median of the six measurements for incyclorotation and excyclorotation) in the study eye and in the fellow eye.

Table A 24: Study eye and fellow eye: Cyclorotation (week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Study Eye - Median monocular subjective cyclorotation			
- N	8	12	20
- Mean +/- SD	10.6 +/- 12.6	-0.2 +/- 2.2	4.1 +/-9.5
- p5, p25, p75, p95	-8.0, 3.8, 15.0, 35.0	-5.0, -0.8, 0.0, 5.0	-6.5, -0.3, 8.8, 26.3
- Median	10.0	0.0	0.0
- Min, Max	-8.0, 35.0	-5.0, 5.0	-8.0, 35.0
- 95% CI Mean	[0.0;21.1]	[-1.6;1.2]	[-0.3;8.6]
- 95% CI Median	[0.0;35.0]	[-1.0;0.0]	[0.0;7.5]
Week 12: Fellow Eye - Median monocular subjective cyclorotation			
- N	8	10	18
- Mean +/- SD	0.6 +/- 1.2	-0.6 +/- 1.6	-0.0 +/-1.5
- p5, p25, p75, p95	0.0, 0.0, 1.3, 2.5	-5.0, 0.0, 0.0, 0.0	-5.0, 0.0, 0.0, 2.5
- Median	0.0	0.0	0.0
- Min, Max	0.0, 2.5	-5.0, 0.0	-5.0, 2.5
- 95% CI Mean	[-0.3;1.6]	[-1.7;0.6]	[-0.8;0.7]
- 95% CI Median	[0.0;2.5]	[-0.5;0.0]	[0.0;0.0]
Week 26: Study Eye - Median monocular subjective cyclorotation			
- N	12	12	24
- Mean +/- SD	-0.5 +/- 24.3	-0.4 +/- 1.0	-0.4 +/-16.8
- p5, p25, p75, p95	-67.5, -1.8, 8.0, 40.0	-2.5, 0.0, 0.0, 0.5	-4.0, -0.5, 0.3, 12.5
- Median	0.0	0.0	0.0
- Min, Max	-67.5, 40.0	-2.5, 0.5	-67.5, 40.0
- 95% CI Mean	[-15.9;15.0]	[-1.0;0.3]	[-7.5;6.7]
- 95% CI Median	[-2.5;11.0]	[0.0;0.0]	[0.0;0.0]
Week 26: Fellow Eye - Median monocular subjective cyclorotation			
- N	12	10	22
- Mean +/- SD	0.6 +/- 1.9	-0.1 +/- 0.3	0.3 +/-1.4
- p5, p25, p75, p95	0.0, 0.0, 0.0, 6.5	-1.0, 0.0, 0.0, 0.0	0.0, 0.0, 0.0, 0.5
- Median	0.0	0.0	0.0
- Min, Max	0.0, 6.5	-1.0, 0.0	-1.0, 6.5
- 95% CI Mean	[-0.6;1.8]	[-0.3;0.1]	[-0.4;0.9]
- 95% CI Median	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]
Week 38: Study Eye - Median monocular subjective cyclorotation			
- N	11	11	22
- Mean +/- SD	1.6 +/- 20.6	0.2 +/- 1.8	0.9 +/-14.3
- p5, p25, p75, p95	-50.0, 0.0, 7.5, 40.0	-2.5, 0.0, 0.0, 5.0	-2.5, 0.0, 5.0, 7.5
- Median	2.5	0.0	0.0
- Min, Max	-50.0, 40.0	-2.5, 5.0	-50.0, 40.0
- 95% CI Mean	[-12.2;15.5]	[-0.9;1.4]	[-5.4;7.3]
- 95% CI Median	[0.0;7.5]	[0.0;0.0]	[0.0;5.0]
Week 38: Fellow Eye - Median monocular subjective cyclorotation			

	Treatment N=13	Control N=15	Total N=28
- N	11	9	20
- Mean +/- SD	0.2 +/- 0.3	-0.3 +/- 2.0	-0.0 +/-1.3
- p5, p25, p75, p95	0.0, 0.0, 0.5, 1.0	-5.0, 0.0, 0.0, 2.5	-2.5, 0.0, 0.0, 1.8
- Median	0.0	0.0	0.0
- Min, Max	0.0, 1.0	-5.0, 2.5	-5.0, 2.5
- 95% CI Mean	[-0.0;0.4]	[-1.8;1.2]	[-0.6;0.6]
- 95% CI Median	[0.0;0.5]	[0.0;0.0]	[0.0;0.0]
Week 52: Study Eye - Median monocular subjective cyclorotation			
- N	12	14	26
- Mean +/- SD	0.2 +/- 25.1	0.5 +/- 1.9	0.3 +/-16.7
- p5, p25, p75, p95	-65.0, 0.0, 5.8, 50.0	0.0, 0.0, 0.0, 7.0	-6.5, 0.0, 0.0, 7.0
- Median	0.0	0.0	0.0
- Min, Max	-65.0, 50.0	0.0, 7.0	-65.0, 50.0
- 95% CI Mean	[-15.8;16.1]	[-0.6;1.6]	[-6.4;7.1]
- 95% CI Median	[0.0;6.5]	[0.0;0.0]	[0.0;0.0]
Week 52: Fellow Eye - Median monocular subjective cyclorotation			
- N	12	12	24
- Mean +/- SD	0.7 +/- 1.5	0.1 +/- 1.8	0.4 +/-1.7
- p5, p25, p75, p95	0.0, 0.0, 0.8, 5.0	-3.5, 0.0, 0.0, 5.0	0.0, 0.0, 0.0, 5.0
- Median	0.0	0.0	0.0
- Min, Max	0.0, 5.0	-3.5, 5.0	-3.5, 5.0
- 95% CI Mean	[-0.3;1.7]	[-1.0;1.3]	[-0.3;1.1]
- 95% CI Median	[0.0;1.5]	[0.0;0.0]	[0.0;0.0]
Week 104: Study Eye - Median monocular subjective cyclorotation			
- N	12	13	25
- Mean +/- SD	0.5 +/- 22.2	0.0 +/- 1.0	0.2 +/-15.0
- p5, p25, p75, p95	-60.0, 0.0, 5.0, 40.0	-2.5, 0.0, 0.0, 2.5	-2.5, 0.0, 0.0, 12.5
- Median	0.0	0.0	0.0
- Min, Max	-60.0, 40.0	-2.5, 2.5	-60.0, 40.0
- 95% CI Mean	[-13.6;14.6]	[-0.6;0.6]	[-6.0;6.4]
- 95% CI Median	[0.0;5.0]	[0.0;0.0]	[0.0;0.0]
Week 104: Fellow Eye - Median monocular subjective cyclorotation			
- N	12	11	23
- Mean +/- SD	0.2 +/- 1.4	0.0 +/- 0.0	0.1 +/-1.0
- p5, p25, p75, p95	-2.5, 0.0, 0.0, 4.0	0.0, 0.0, 0.0, 0.0	0.0, 0.0, 0.0, 1.0
- Median	0.0	0.0	0.0
- Min, Max	-2.5, 4.0	0.0, 0.0	-2.5, 4.0
- 95% CI Mean	[-0.7;1.1]	[0.0;0.0]	[-0.3;0.6]
- 95% CI Median	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]

Table A 25 shows the assessment of the binocular vision (Bagolini test and the Titmus test) in week 12, 26, 38, 52 and 104).

Table A 25: Binocular Vision (week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Bagolini Test			
- Simultaneous	1 (12.5%)	6 (50.0%)	7 (35.0%)
- Exclusion right eye	2 (25.0%)	2 (16.7%)	4 (20.0%)
- Exclusion left eye	4 (50.0%)	4 (33.3%)	8 (40.0%)
- Not possible	1 (12.5%)	0 (0.0%)	1 (5.0%)
- missing	5	3	8
Week 12: Titmus Test			
- Positive	0 (0.0%)	5 (41.7%)	5 (25.0%)
- Negative	8 (100.0%)	7 (58.3%)	15 (75.0%)
- missing	5	3	8
Week 26: Bagolini Test			
- Simultaneous	5 (41.7%)	7 (58.3%)	12 (50.0%)
- Exclusion right eye	4 (33.3%)	1 (8.3%)	5 (20.8%)
- Exclusion left eye	3 (25.0%)	4 (33.3%)	7 (29.2%)
- missing	1	3	4
Week 26: Titmus Test			
- Positive	2 (16.7%)	6 (50.0%)	8 (33.3%)
- Negative	10 (83.3%)	6 (50.0%)	16 (66.7%)
- missing	1	3	4
Week 38: Bagolini Test			
- Simultaneous	5 (41.7%)	6 (54.5%)	11 (47.8%)
- Exclusion right eye	5 (41.7%)	2 (18.2%)	7 (30.4%)
- Exclusion left eye	2 (16.7%)	3 (27.3%)	5 (21.7%)
- missing	1	4	5
Week 38: Titmus Test			
- Positive	4 (33.3%)	3 (27.3%)	7 (30.4%)
- Negative	8 (66.7%)	8 (72.7%)	16 (69.6%)
- missing	1	4	5
Week 52: Bagolini Test			
- Simultaneous	5 (41.7%)	8 (57.1%)	13 (50.0%)
- Exclusion right eye	4 (33.3%)	2 (14.3%)	6 (23.1%)
- Exclusion left eye	3 (25.0%)	4 (28.6%)	7 (26.9%)
- missing	1	1	2
Week 52: Titmus Test			
- Positive	3 (25.0%)	6 (42.9%)	9 (34.6%)
- Negative	9 (75.0%)	8 (57.1%)	17 (65.4%)
- missing	1	1	2
Week 104: Bagolini Test			
- Simultaneous	5 (41.7%)	8 (61.5%)	13 (52.0%)
- Exclusion right eye	4 (33.3%)	2 (15.4%)	6 (24.0%)
- Exclusion left eye	3 (25.0%)	3 (23.1%)	6 (24.0%)
- missing	1	2	3
Week 104: Titmus Test			
- Positive	4 (33.3%)	7 (53.8%)	11 (44.0%)
- Negative	8 (66.7%)	6 (46.2%)	14 (56.0%)
- missing	1	2	3

Table A 26 respectively Table A 27 summarizes the refraction measured in the in the study eye respectively in the fellow eye.

Table A 26: Study eye: Refraction (week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Study Eye - Sphere			
- N	8	12	20
- Mean +/- SD	-0.9 +/- 5.9	2.4 +/- 2.3	1.1 +/-4.3
- p5, p25, p75, p95	-10.0, -3.3, 0.0, 11.0	-0.5, 0.8, 4.0, 7.0	-7.5, -0.6, 3.0, 9.0
- Median	-1.0	1.6	0.8
- Min, Max	-10.0, 11.0	-0.5, 7.0	-10.0, 11.0
- 95% CI Mean	[-5.9;4.0]	[1.0;3.9]	[-0.9;3.1]
- 95% CI Median	[-5.0;11.0]	[0.5;5.0]	[-0.5;3.0]
Week 12: Study Eye - Cylinder			
- N	8	12	20
- Mean +/- SD	2.4 +/- 3.4	0.1 +/- 0.8	1.1 +/-2.5
- p5, p25, p75, p95	0.0, 0.3, 3.8, 10.0	-1.5, 0.0, 0.6, 1.5	-1.3, 0.0, 0.9, 7.3
- Median	0.8	0.0	0.5
- Min, Max	0.0, 10.0	-1.5, 1.5	-1.5, 10.0
- 95% CI Mean	[-0.4;5.3]	[-0.4;0.7]	[-0.1;2.2]
- 95% CI Median	[0.0;10.0]	[0.0;0.8]	[0.0;0.8]
Week 12: Study Eye - Axis			
- N	8	12	20
- Mean +/- SD	95.6 +/- 68.3	80.4 +/- 77.3	86.5 +/-72.4
- p5, p25, p75, p95	0.0, 42.5, 155.0, 180.0	0.0, 0.0, 160.0, 180.0	0.0, 0.0, 155.0, 180.0
- Median	95.0	92.5	92.5
- Min, Max	0.0, 180.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[38.5;152.7]	[31.3;129.5]	[52.6;120.4]
- 95% CI Median	[0.0;180.0]	[0.0;170.0]	[0.0;150.0]
Week 26: Study Eye - Sphere			
- N	12	12	24
- Mean +/- SD	1.5 +/- 2.6	1.8 +/- 2.2	1.6 +/-2.4
- p5, p25, p75, p95	-1.8, -1.3, 4.0, 5.0	-0.5, 0.0, 3.0, 7.0	-1.8, 0.0, 3.0, 5.0
- Median	1.4	1.1	1.3
- Min, Max	-1.8, 5.0	-0.5, 7.0	-1.8, 7.0
- 95% CI Mean	[-0.2;3.1]	[0.4;3.2]	[0.6;2.7]
- 95% CI Median	[-1.5;5.0]	[0.0;3.0]	[0.0;3.0]
Week 26: Study Eye - Cylinder			
- N	12	12	24
- Mean +/- SD	-0.0 +/- 1.5	0.0 +/- 0.9	0.0 +/-1.2
- p5, p25, p75, p95	-3.0, -0.8, 1.0, 1.5	-1.5, -0.6, 0.6, 1.5	-2.5, -0.6, 1.0, 1.5
- Median	0.6	0.0	0.3
- Min, Max	-3.0, 1.5	-1.5, 1.5	-3.0, 1.5
- 95% CI Mean	[-1.0;0.9]	[-0.5;0.6]	[-0.5;0.5]
- 95% CI Median	[-1.5;1.0]	[-0.8;0.8]	[0.0;1.0]
Week 26: Study Eye - Axis			
- N	12	12	24
- Mean +/- SD	85.0 +/- 54.4	90.0 +/- 73.4	87.5 +/-63.2
- p5, p25, p75, p95	0.0, 42.5, 117.5, 160.0	0.0, 10.0, 165.0, 180.0	0.0, 22.5, 142.5, 180.0
- Median	95.0	105.0	97.5
- Min, Max	0.0, 160.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[50.4;119.6]	[43.4;136.6]	[60.8;114.2]
- 95% CI Median	[25.0;125.0]	[0.0;170.0]	[50.0;125.0]
Week 38: Study Eye - Sphere			
- N	12	11	23

	Treatment N=13	Control N=15	Total N=28
- Mean +/- SD	0.9 +/- 3.1	2.6 +/- 2.9	1.7 +/-3.1
- p5, p25, p75, p95	-2.8, -1.8, 3.8, 6.0	-1.0, 0.0, 4.5, 8.0	-2.0, -1.0, 4.5, 7.0
- Median	0.0	1.5	1.3
- Min, Max	-2.8, 6.0	-1.0, 8.0	-2.8, 8.0
- 95% CI Mean	[-1.1;2.9]	[0.6;4.5]	[0.4;3.0]
- 95% CI Median	[-2.0;4.5]	[0.0;7.0]	[-0.5;3.0]
Week 38: Study Eye - Cylinder			
- N	12	11	23
- Mean +/- SD	0.5 +/- 1.5	0.1 +/- 1.0	0.3 +/-1.2
- p5, p25, p75, p95	-3.0, 0.0, 1.3, 2.5	-1.5, -0.5, 0.5, 2.0	-1.5, -0.5, 1.0, 2.0
- Median	0.9	0.0	0.0
- Min, Max	-3.0, 2.5	-1.5, 2.0	-3.0, 2.5
- 95% CI Mean	[-0.4;1.4]	[-0.6;0.8]	[-0.2;0.8]
- 95% CI Median	[0.0;1.5]	[-0.5;1.5]	[0.0;1.0]
Week 38: Study Eye - Axis			
- N	12	11	23
- Mean +/- SD	84.2 +/- 63.1	98.6 +/- 75.4	91.1 +/-68.1
- p5, p25, p75, p95	0.0, 22.5, 125.0, 180.0	0.0, 0.0, 170.0, 180.0	0.0, 0.0, 160.0, 180.0
- Median	92.5	100.0	100.0
- Min, Max	0.0, 180.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[44.1;124.3]	[48.0;149.3]	[61.6;120.5]
- 95% CI Median	[0.0;130.0]	[0.0;180.0]	[45.0;155.0]
Week 52: Study Eye - Sphere			
- N	11	14	25
- Mean +/- SD	-0.3 +/- 3.2	1.5 +/- 2.7	0.7 +/-3.0
- p5, p25, p75, p95	-7.0, -2.0, 1.5, 4.5	-4.0, 0.5, 3.0, 7.0	-4.0, -1.0, 1.5, 5.0
- Median	-1.0	1.0	1.0
- Min, Max	-7.0, 4.5	-4.0, 7.0	-7.0, 7.0
- 95% CI Mean	[-2.4;1.9]	[-0.1;3.1]	[-0.5;2.0]
- 95% CI Median	[-2.0;4.3]	[0.5;4.5]	[-1.0;1.3]
Week 52: Study Eye - Cylinder			
- N	11	14	25
- Mean +/- SD	0.8 +/- 3.0	0.0 +/- 1.0	0.4 +/-2.1
- p5, p25, p75, p95	-4.0, -1.0, 2.0, 8.0	-1.0, -0.8, 0.5, 2.0	-1.5, -0.8, 1.0, 2.5
- Median	0.8	-0.3	0.0
- Min, Max	-4.0, 8.0	-1.0, 2.0	-4.0, 8.0
- 95% CI Mean	[-1.2;2.8]	[-0.6;0.6]	[-0.5;1.2]
- 95% CI Median	[-1.0;2.5]	[-0.8;1.0]	[-0.8;1.0]
Week 52: Study Eye - Axis			
- N	11	14	25
- Mean +/- SD	91.4 +/- 43.1	112.1 +/- 61.3	103.0 +/-54.0
- p5, p25, p75, p95	0.0, 70.0, 120.0, 170.0	0.0, 90.0, 170.0, 180.0	0.0, 80.0, 150.0, 180.0
- Median	95.0	100.0	100.0
- Min, Max	0.0, 170.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[62.4;120.3]	[76.8;147.5]	[80.7;125.3]
- 95% CI Median	[70.0;125.0]	[90.0;180.0]	[90.0;125.0]
Week 104: Study Eye - Sphere			
- N	12	13	25
- Mean +/- SD	-1.1 +/- 4.5	1.0 +/- 2.7	-0.0 +/-3.8
- p5, p25, p75, p95	-12.0, -1.6, 1.0, 4.8	-4.0, 0.0, 1.5, 7.0	-7.0, -1.0, 1.3, 4.8
- Median	-0.8	1.0	0.5
- Min, Max	-12.0, 4.8	-4.0, 7.0	-12.0, 7.0
- 95% CI Mean	[-4.0;1.8]	[-0.6;2.6]	[-1.6;1.5]
- 95% CI Median	[-1.8;1.3]	[-0.5;2.8]	[-1.0;1.3]
Week 104: Study Eye - Cylinder			
- N	12	13	25

	Treatment N=13	Control N=15	Total N=28
- Mean +/- SD	2.5 +/- 5.7	0.3 +/- 1.1	1.4 +/-4.1
- p5, p25, p75, p95	-3.0, -0.8, 3.3, 18.0	-1.0, -0.5, 0.5, 3.0	-1.0, -0.5, 1.5, 8.0
- Median	0.9	0.0	0.5
- Min, Max	-3.0, 18.0	-1.0, 3.0	-3.0, 18.0
- 95% CI Mean	[-1.1;6.1]	[-0.4;1.0]	[-0.3;3.0]
- 95% CI Median	[-1.0;5.0]	[-0.5;1.5]	[-0.5;1.0]
Week 104: Study Eye - Axis			
- N	12	13	25
- Mean +/- SD	100.4 +/- 45.1	121.9 +/- 67.6	111.6 +/-57.7
- p5, p25, p75, p95	0.0, 77.5, 122.5, 175.0	0.0, 90.0, 180.0, 180.0	0.0, 85.0, 170.0, 180.0
- Median	100.0	160.0	100.0
- Min, Max	0.0, 175.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[71.8;129.1]	[81.1;162.8]	[87.8;135.4]
- 95% CI Median	[75.0;125.0]	[85.0;180.0]	[90.0;160.0]

Table A 27: Fellow eye: Refraction (week 12, 26, 38, 52 and 104).

	Treatment N=13	**Control N=15**	**Total N=28**
Week 12: Fellow Eye - Sphere			
- N	8	11	19
- Mean +/- SD	0.2 +/- 2.3	1.3 +/- 2.3	0.8 +/-2.3
- p5, p25, p75, p95	-3.5, -1.1, 1.5, 4.0	-1.0, 0.0, 1.5, 7.0	-3.5, 0.0, 1.5, 7.0
- Median	0.0	0.3	0.0
- Min, Max	-3.5, 4.0	-1.0, 7.0	-3.5, 7.0
- 95% CI Mean	[-1.8;2.1]	[-0.3;2.8]	[-0.3;1.9]
- 95% CI Median	[-2.0;4.0]	[0.0;4.0]	[0.0;1.5]
Week 12: Fellow Eye - Cylinder			
- N	8	11	19
- Mean +/- SD	0.8 +/- 1.1	0.2 +/- 0.5	0.4 +/-0.9
- p5, p25, p75, p95	-0.8, 0.1, 1.3, 3.0	-1.0, 0.0, 0.5, 1.0	-1.0, 0.0, 0.8, 3.0
- Median	0.6	0.0	0.3
- Min, Max	-0.8, 3.0	-1.0, 1.0	-1.0, 3.0
- 95% CI Mean	[-0.2;1.7]	[-0.2;0.5]	[0.0;0.8]
- 95% CI Median	[0.0;3.0]	[0.0;0.8]	[0.0;0.8]
Week 12: Fellow Eye - Axis			
- N	8	11	19
- Mean +/- SD	69.4 +/- 63.9	47.3 +/- 64.8	56.6 +/-63.6
- p5, p25, p75, p95	0.0, 7.5, 125.0, 160.0	0.0, 0.0, 100.0, 160.0	0.0, 0.0, 110.0, 160.0
- Median	65.0	0.0	20.0
- Min, Max	0.0, 160.0	0.0, 160.0	0.0, 160.0
- 95% CI Mean	[15.9;122.8]	[3.7;90.8]	[25.9;87.3]
- 95% CI Median	[5.0;160.0]	[0.0;150.0]	[0.0;110.0]
Week 26: Fellow Eye - Sphere			
- N	12	12	24
- Mean +/- SD	-0.4 +/- 1.7	2.1 +/- 3.0	0.9 +/-2.7
- p5, p25, p75, p95	-3.5, -1.5, 0.8, 2.0	-1.0, 0.0, 4.3, 8.0	-2.0, -0.8, 1.6, 7.0
- Median	-0.3	1.1	0.0
- Min, Max	-3.5, 2.0	-1.0, 8.0	-3.5, 8.0
- 95% CI Mean	[-1.4;0.7]	[0.2;4.1]	[-0.3;2.0]
- 95% CI Median	[-2.0;1.0]	[0.0;5.0]	[-0.3;1.3]
Week 26: Fellow Eye - Cylinder			
- N	11	12	23
- Mean +/- SD	0.4 +/- 0.8	-0.1 +/- 0.6	0.2 +/-0.7
- p5, p25, p75, p95	-0.8, 0.0, 1.0, 2.0	-1.5, 0.0, 0.3, 0.8	-1.0, 0.0, 0.5, 1.0
- Median	0.5	0.0	0.0
- Min, Max	-0.8, 2.0	-1.5, 0.8	-1.5, 2.0
- 95% CI Mean	[-0.2;0.9]	[-0.5;0.3]	[-0.2;0.5]
- 95% CI Median	[0.0;1.0]	[0.0;0.5]	[0.0;0.5]
Week 26: Fellow Eye - Axis			
- N	11	12	23
- Mean +/- SD	96.8 +/- 69.9	40.4 +/- 61.2	67.4 +/-70.2
- p5, p25, p75, p95	0.0, 0.0, 155.0, 170.0	0.0, 0.0, 77.5, 160.0	0.0, 0.0, 150.0, 170.0
- Median	110.0	0.0	65.0
- Min, Max	0.0, 170.0	0.0, 160.0	0.0, 170.0
- 95% CI Mean	[49.9;143.8]	[1.5;79.3]	[37.1;97.7]
- 95% CI Median	[0.0;170.0]	[0.0;90.0]	[0.0;150.0]
Week 38: Fellow Eye - Sphere			
- N	12	10	22
- Mean +/- SD	-0.5 +/- 1.2	1.8 +/- 2.5	0.5 +/-2.2
- p5, p25, p75, p95	-2.0, -1.5, 0.8, 1.5	-0.5, 0.0, 3.5, 7.0	-1.5, -1.0, 1.0, 5.0
- Median	-1.0	1.0	0.3
- Min, Max	-2.0, 1.5	-0.5, 7.0	-2.0, 7.0
- 95% CI Mean	[-1.3;0.2]	[0.0;3.6]	[-0.5;1.5]

	Treatment N=13	Control N=15	Total N=28
- 95% CI Median	[-1.5;1.0]	[-0.5;5.0]	[-1.0;1.0]
Week 38: Fellow Eye - Cylinder			
- N	12	10	22
- Mean +/- SD	0.3 +/- 0.9	0.1 +/- 0.8	0.2 +/-0.8
- p5, p25, p75, p95	-0.8, -0.5, 0.9, 2.0	-1.5, 0.0, 0.5, 1.0	-1.0, -0.5, 0.8, 1.5
- Median	0.0	0.3	0.0
- Min, Max	-0.8, 2.0	-1.5, 1.0	-1.5, 2.0
- 95% CI Mean	[-0.3;0.8]	[-0.5;0.6]	[-0.2;0.6]
- 95% CI Median	[-0.5;1.0]	[-1.0;0.8]	[0.0;0.8]
Week 38: Fellow Eye - Axis			
- N	12	10	22
- Mean +/- SD	87.1 +/- 68.8	68.5 +/- 72.0	78.6 +/-69.2
- p5, p25, p75, p95	0.0, 5.0, 145.0, 180.0	0.0, 0.0, 150.0, 180.0	0.0, 0.0, 150.0, 180.0
- Median	100.0	42.5	87.5
- Min, Max	0.0, 180.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[43.4;130.8]	[17.0;120.0]	[47.9;109.3]
- 95% CI Median	[0.0;150.0]	[0.0;160.0]	[10.0;150.0]
Week 52: Fellow Eye - Sphere			
- N	12	13	25
- Mean +/- SD	-0.3 +/- 1.5	1.9 +/- 2.2	0.8 +/-2.1
- p5, p25, p75, p95	-3.0, -1.4, 1.0, 1.5	-0.5, 1.0, 3.0, 7.0	-2.5, -0.5, 1.0, 5.0
- Median	0.0	1.0	1.0
- Min, Max	-3.0, 1.5	-0.5, 7.0	-3.0, 7.0
- 95% CI Mean	[-1.2;0.7]	[0.6;3.2]	[-0.0;1.7]
- 95% CI Median	[-1.5;1.0]	[0.0;3.5]	[0.0;1.0]
Week 52: Fellow Eye - Cylinder			
- N	11	13	24
- Mean +/- SD	0.4 +/- 0.9	0.1 +/- 0.8	0.2 +/-0.8
- p5, p25, p75, p95	-1.0, 0.0, 1.0, 2.0	-1.5, 0.0, 0.5, 1.5	-1.0, 0.0, 0.6, 1.5
- Median	0.0	0.0	0.0
- Min, Max	-1.0, 2.0	-1.5, 1.5	-1.5, 2.0
- 95% CI Mean	[-0.2;1.0]	[-0.4;0.6]	[-0.1;0.6]
- 95% CI Median	[0.0;1.5]	[-0.5;0.5]	[0.0;0.5]
Week 52: Fellow Eye - Axis			
- N	11	13	24
- Mean +/- SD	64.5 +/- 66.2	67.3 +/- 68.2	66.0 +/-65.9
- p5, p25, p75, p95	0.0, 0.0, 110.0, 180.0	0.0, 0.0, 130.0, 165.0	0.0, 0.0, 120.0, 165.0
- Median	80.0	65.0	72.5
- Min, Max	0.0, 180.0	0.0, 165.0	0.0, 180.0
- 95% CI Mean	[20.0;109.0]	[26.1;108.5]	[38.2;93.9]
- 95% CI Median	[0.0;150.0]	[0.0;150.0]	[0.0;110.0]
Week 104: Fellow Eye - Sphere			
- N	12	12	24
- Mean +/- SD	-0.4 +/- 1.4	2.1 +/- 2.5	0.9 +/-2.4
- p5, p25, p75, p95	-3.0, -1.6, 0.9, 1.3	-1.0, 0.9, 3.9, 7.0	-2.0, -0.8, 1.3, 5.8
- Median	-0.1	1.1	0.9
- Min, Max	-3.0, 1.3	-1.0, 7.0	-3.0, 7.0
- 95% CI Mean	[-1.3;0.5]	[0.6;3.7]	[-0.1;1.8]
- 95% CI Median	[-1.8;1.0]	[0.8;4.0]	[-0.5;1.3]
Week 104: Fellow Eye - Cylinder			
- N	12	12	24
- Mean +/- SD	0.5 +/- 1.0	0.3 +/- 1.3	0.4 +/-1.2
- p5, p25, p75, p95	-1.0, 0.0, 1.5, 2.0	-1.5, -0.9, 1.0, 3.0	-1.0, -0.4, 1.3, 2.0
- Median	0.0	0.3	0.0
- Min, Max	-1.0, 2.0	-1.5, 3.0	-1.5, 3.0
- 95% CI Mean	[-0.2;1.1]	[-0.5;1.2]	[-0.1;0.9]

	Treatment N=13	Control N=15	Total N=28
- 95% CI Median	[0.0;2.0]	[-1.0;1.5]	[0.0;1.0]
Week 104: Fellow Eye - Axis			
- N	12	12	24
- Mean +/- SD	63.3 +/- 67.2	89.2 +/- 73.4	76.3 +/-70.1
- p5, p25, p75, p95	0.0, 0.0, 120.0, 180.0	0.0, 12.5, 162.5, 180.0	0.0, 0.0, 145.0, 180.0
- Median	50.0	77.5	72.5
- Min, Max	0.0, 180.0	0.0, 180.0	0.0, 180.0
- 95% CI Mean	[20.6;106.0]	[42.6;135.8]	[46.7;105.8]
- 95% CI Median	[0.0;130.0]	[10.0;165.0]	[10.0;140.0]

11.5 Control Examinations: Eye specific Quality of Life

Table A 28 shows the 12 sub scales and the composite score of the NEI-VFQ questionnaire, measured at the control examinations in week 26, 52, 104.

Table A 28: Eye specific Quality of Life: sub scales and total score (week 26, 52, 104).

	Treatment N=13	Control N=15	Total N=28
Week 26: General Health			
- N	10	10	20
- Mean +/- SD	60.0 +/- 17.5	45.0 +/- 25.8	52.5 +/-22.8
- p5, p25, p75, p95	25.0, 50.0, 75.0, 75.0	0.0, 25.0, 50.0, 100.0	12.5, 50.0, 75.0, 87.5
- Median	62.5	50.0	50.0
- Min, Max	25.0, 75.0	0.0, 100.0	0.0, 100.0
- 95% CI Mean	[47.5;72.5]	[26.5;63.5]	[41.8;63.2]
- 95% CI Median	[50.0;75.0]	[25.0;50.0]	[50.0;75.0]
Week 26: General Vision			
- N	10	10	20
- Mean +/- SD	56.0 +/- 18.4	32.0 +/- 14.0	44.0 +/-20.1
- p5, p25, p75, p95	20.0, 40.0, 60.0, 80.0	20.0, 20.0, 40.0, 60.0	20.0, 20.0, 60.0, 80.0
- Median	60.0	30.0	40.0
- Min, Max	20.0, 80.0	20.0, 60.0	20.0, 80.0
- 95% CI Mean	[42.9;69.1]	[22.0;42.0]	[34.6;53.4]
- 95% CI Median	[40.0;80.0]	[20.0;40.0]	[20.0;60.0]
Week 26: Ocular Pain			
- N	10	10	20
- Mean +/- SD	91.3 +/- 6.0	91.3 +/- 20.5	91.3 +/-14.7
- p5, p25, p75, p95	87.5, 87.5, 100.0, 100.0	37.5, 100.0, 100.0, 100.0	56.3, 87.5, 100.0, 100.0
- Median	87.5	100.0	100.0
- Min, Max	87.5, 100.0	37.5, 100.0	37.5, 100.0
- 95% CI Mean	[86.9;95.6]	[76.6;105.9]	[84.4;98.1]
- 95% CI Median	[87.5;100.0]	[75.0;100.0]	[87.5;100.0]
Week 26: Near Activities			
- N	10	10	20
- Mean +/- SD	35.8 +/- 25.2	27.5 +/- 18.9	31.7 +/-22.1
- p5, p25, p75, p95	0.0, 16.7, 50.0, 75.0	8.3, 16.7, 41.7, 66.7	4.2, 16.7, 45.8, 75.0
- Median	33.3	16.7	29.2
- Min, Max	0.0, 75.0	8.3, 66.7	0.0, 75.0
- 95% CI Mean	[17.8;53.8]	[14.0;41.0]	[21.3;42.0]
- 95% CI Median	[8.3;75.0]	[16.7;50.0]	[16.7;41.7]
Week 26: Distance Activities			
- N	10	10	20
- Mean +/- SD	40.0 +/- 29.1	37.1 +/- 19.7	38.5 +/-24.2
- p5, p25, p75, p95	8.3, 16.7, 50.0, 100.0	8.3, 25.0, 41.7, 75.0	8.3, 20.8, 50.0, 87.5

	Treatment N=13	Control N=15	Total N=28
- Median	29.2	39.6	35.4
- Min, Max	8.3, 100.0	8.3, 75.0	8.3, 100.0
- 95% CI Mean	[19.2;60.8]	[23.0;51.2]	[27.2;49.9]
- 95% CI Median	[16.7;75.0]	[16.7;58.3]	[25.0;50.0]
Week 26: Vision Specific: Social Functioning			
- N	10	10	20
- Mean +/- SD	43.8 +/- 27.2	41.3 +/- 24.3	42.5 +/-25.1
- p5, p25, p75, p95	12.5, 25.0, 62.5, 100.0	0.0, 37.5, 62.5, 75.0	6.3, 25.0, 62.5, 87.5
- Median	37.5	37.5	37.5
- Min, Max	12.5, 100.0	0.0, 75.0	0.0, 100.0
- 95% CI Mean	[24.3;63.2]	[23.8;58.7]	[30.7;54.3]
- 95% CI Median	[25.0;75.0]	[12.5;75.0]	[25.0;62.5]
Week 26: Vision Specific: Mental Health			
- N	10	10	20
- Mean +/- SD	38.8 +/- 25.7	38.8 +/- 27.0	38.8 +/-25.6
- p5, p25, p75, p95	6.3, 18.8, 62.5, 81.3	0.0, 12.5, 56.3, 87.5	3.1, 18.8, 56.3, 84.4
- Median	31.3	40.6	34.4
- Min, Max	6.3, 81.3	0.0, 87.5	0.0, 87.5
- 95% CI Mean	[20.4;57.1]	[19.5;58.0]	[26.8;50.7]
- 95% CI Median	[18.8;75.0]	[12.5;56.3]	[18.8;56.3]
Week 26: Vision Specific: Role Difficulties			
- N	10	10	20
- Mean +/- SD	45.0 +/- 31.3	55.0 +/- 29.0	50.0 +/-29.8
- p5, p25, p75, p95	0.0, 25.0, 75.0, 87.5	12.5, 37.5, 75.0, 100.0	0.0, 25.0, 75.0, 93.8
- Median	50.0	50.0	50.0
- Min, Max	0.0, 87.5	12.5, 100.0	0.0, 100.0
- 95% CI Mean	[22.6;67.4]	[34.3;75.7]	[36.1;63.9]
- 95% CI Median	[0.0;75.0]	[25.0;87.5]	[25.0;75.0]
Week 26: Vision Specific: Dependency			
- N	10	10	20
- Mean +/- SD	47.5 +/- 32.9	31.7 +/- 30.4	39.6 +/-31.9
- p5, p25, p75, p95	0.0, 25.0, 75.0, 100.0	0.0, 8.3, 58.3, 83.3	0.0, 8.3, 70.8, 91.7
- Median	41.7	20.8	33.3
- Min, Max	0.0, 100.0	0.0, 83.3	0.0, 100.0
- 95% CI Mean	[24.0;71.0]	[9.9;53.4]	[24.7;54.5]
- 95% CI Median	[8.3;75.0]	[0.0;66.7]	[8.3;66.7]
Week 26: Color Vision			
- N	10	10	20
- Mean +/- SD	62.5 +/- 41.2	72.5 +/- 27.5	67.5 +/-34.5
- p5, p25, p75, p95	0.0, 25.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0	12.5, 37.5, 100.0, 100.0
- Median	75.0	75.0	75.0
- Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
- 95% CI Mean	[33.0;92.0]	[52.8;92.2]	[51.3;83.7]
- 95% CI Median	[25.0;100.0]	[50.0;100.0]	[50.0;100.0]
Week 26: Peripheral Vision			
- N	10	10	20
- Mean +/- SD	55.0 +/- 28.4	65.0 +/- 37.6	60.0 +/-32.8
- p5, p25, p75, p95	25.0, 25.0, 75.0, 100.0	0.0, 25.0, 100.0, 100.0	12.5, 25.0, 100.0, 100.0
- Median	50.0	75.0	50.0
- Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0
- 95% CI Mean	[34.7;75.3]	[38.1;91.9]	[44.6;75.4]
- 95% CI Median	[25.0;100.0]	[25.0;100.0]	[25.0;100.0]
Week 26: Composite Score			

	Treatment N=13	Control N=15	Total N=28
- N	10	10	20
- Mean +/- SD	51.6 +/- 18.9	49.1 +/- 15.9	50.3 +/-17.1
- p5, p25, p75, p95	27.7, 36.3, 69.7, 79.9	28.3, 37.8, 64.1, 77.1	28.0, 37.4, 66.7, 78.5
- Median	48.7	44.6	44.6
- Min, Max	27.7, 79.9	28.3, 77.1	27.7, 79.9
- 95% CI Mean	[38.0;65.1]	[37.7;60.4]	[42.3;58.3]
- 95% CI Median	[29.3;73.5]	[36.9;69.2]	[37.8;64.1]
Week 52: General Health			
- N	12	14	26
- Mean +/- SD	43.8 +/- 21.7	37.5 +/- 19.0	40.4 +/-20.1
- p5, p25, p75, p95	0.0, 25.0, 50.0, 75.0	0.0, 25.0, 50.0, 75.0	0.0, 25.0, 50.0, 75.0
- Median	50.0	37.5	50.0
- Min, Max	0.0, 75.0	0.0, 75.0	0.0, 75.0
- 95% CI Mean	[30.0;57.5]	[26.5;48.5]	[32.3;48.5]
- 95% CI Median	[25.0;50.0]	[25.0;50.0]	[25.0;50.0]
Week 52: General Vision			
- N	12	14	26
- Mean +/- SD	48.3 +/- 18.0	38.6 +/- 16.6	43.1 +/-17.6
- p5, p25, p75, p95	20.0, 40.0, 60.0, 80.0	20.0, 20.0, 60.0, 60.0	20.0, 20.0, 60.0, 60.0
- Median	50.0	40.0	40.0
- Min, Max	20.0, 80.0	20.0, 60.0	20.0, 80.0
- 95% CI Mean	[36.9;59.8]	[29.0;48.1]	[36.0;50.2]
- 95% CI Median	[40.0;60.0]	[20.0;60.0]	[40.0;60.0]
Week 52: Ocular Pain			
- N	12	14	26
- Mean +/- SD	85.4 +/- 14.9	89.3 +/- 16.2	87.5 +/-15.4
- p5, p25, p75, p95	62.5, 75.0, 100.0, 100.0	50.0, 87.5, 100.0, 100.0	62.5, 75.0, 100.0, 100.0
- Median	87.5	100.0	93.8
- Min, Max	62.5, 100.0	50.0, 100.0	50.0, 100.0
- 95% CI Mean	[75.9;94.9]	[80.0;98.6]	[81.3;93.7]
- 95% CI Median	[75.0;100.0]	[87.5;100.0]	[75.0;100.0]
Week 52: Near Activities			
- N	12	14	26
- Mean +/- SD	38.9 +/- 23.4	26.2 +/- 14.6	32.1 +/-19.8
- p5, p25, p75, p95	0.0, 29.2, 45.8, 91.7	8.3, 16.7, 33.3, 58.3	8.3, 16.7, 41.7, 66.7
- Median	33.3	25.0	33.3
- Min, Max	0.0, 91.7	8.3, 58.3	0.0, 91.7
- 95% CI Mean	[24.0;53.8]	[17.8;34.6]	[24.0;40.1]
- 95% CI Median	[25.0;50.0]	[16.7;33.3]	[16.7;33.3]
Week 52: Distance Activities			
- N	12	14	26
- Mean +/- SD	33.7 +/- 26.1	33.0 +/- 16.4	33.3 +/-21.0
- p5, p25, p75, p95	0.0, 20.8, 39.6, 91.7	16.7, 16.7, 41.7, 66.7	8.3, 16.7, 41.7, 75.0
- Median	25.0	29.2	25.0
- Min, Max	0.0, 91.7	16.7, 66.7	0.0, 91.7
- 95% CI Mean	[17.1;50.3]	[23.6;42.5]	[24.9;41.8]
- 95% CI Median	[16.7;41.7]	[16.7;41.7]	[25.0;41.7]
Week 52: Vision Specific: Social Functioning			
- N	12	14	26
- Mean +/- SD	44.8 +/- 26.9	42.0 +/- 23.3	43.3 +/-24.6
- p5, p25, p75, p95	12.5, 18.8, 62.5, 100.0	12.5, 25.0, 50.0, 87.5	12.5, 25.0, 62.5, 87.5
- Median	43.8	37.5	37.5
- Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0
- 95% CI Mean	[27.7;61.9]	[28.5;55.4]	[33.4;53.2]
- 95% CI Median	[12.5;62.5]	[25.0;75.0]	[25.0;62.5]

	Treatment N=13	Control N=15	Total N=28
Week 52: Vision Specific: Mental Health			
- N	12	14	26
- Mean +/- SD	41.1 +/- 27.9	38.8 +/- 23.3	39.9 +/-25.0
- p5, p25, p75, p95	6.3, 25.0, 56.3, 100.0	6.3, 25.0, 56.3, 87.5	6.3, 25.0, 56.3, 87.5
- Median	34.4	37.5	37.5
- Min, Max	6.3, 100.0	6.3, 87.5	6.3, 100.0
- 95% CI Mean	[23.4;58.9]	[25.4;52.3]	[29.8;50.0]
- 95% CI Median	[25.0;62.5]	[25.0;56.3]	[25.0;50.0]
Week 52: Vision Specific: Role Difficulties			
- N	12	14	26
- Mean +/- SD	42.7 +/- 34.7	46.4 +/- 29.6	44.7 +/-31.5
- p5, p25, p75, p95	0.0, 6.3, 75.0, 87.5	0.0, 25.0, 75.0, 100.0	0.0, 25.0, 75.0, 87.5
- Median	43.8	50.0	50.0
- Min, Max	0.0, 87.5	0.0, 100.0	0.0, 100.0
- 95% CI Mean	[20.6;64.8]	[29.3;63.5]	[32.0;57.4]
- 95% CI Median	[0.0;75.0]	[25.0;75.0]	[25.0;75.0]
Week 52: Vision Specific: Dependency			
- N	12	14	26
- Mean +/- SD	38.2 +/- 34.9	33.9 +/- 34.4	35.9 +/-34.0
- p5, p25, p75, p95	0.0, 8.3, 62.5, 100.0	0.0, 8.3, 58.3, 91.7	0.0, 8.3, 58.3, 91.7
- Median	33.3	16.7	25.0
- Min, Max	0.0, 100.0	0.0, 91.7	0.0, 100.0
- 95% CI Mean	[16.0;60.4]	[14.1;53.8]	[22.2;49.6]
- 95% CI Median	[8.3;83.3]	[8.3;83.3]	[8.3;50.0]
Week 52: Color Vision			
- N	12	14	26
- Mean +/- SD	64.6 +/- 29.1	73.2 +/- 28.5	69.2 +/-28.6
- p5, p25, p75, p95	25.0, 50.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0
- Median	50.0	75.0	75.0
- Min, Max	25.0, 100.0	25.0, 100.0	25.0, 100.0
- 95% CI Mean	[46.1;83.1]	[56.7;89.7]	[57.7;80.8]
- 95% CI Median	[50.0;100.0]	[50.0;100.0]	[50.0;100.0]
Week 52: Peripheral Vision			
- N	12	14	26
- Mean +/- SD	60.4 +/- 29.1	66.1 +/- 23.2	63.5 +/-25.7
- p5, p25, p75, p95	25.0, 37.5, 87.5, 100.0	25.0, 50.0, 75.0, 100.0	25.0, 50.0, 75.0, 100.0
- Median	50.0	62.5	50.0
- Min, Max	25.0, 100.0	25.0, 100.0	25.0, 100.0
- 95% CI Mean	[41.9;78.9]	[52.7;79.5]	[53.1;73.9]
- 95% CI Median	[25.0;100.0]	[50.0;100.0]	[50.0;75.0]
Week 52: Composite Score			
- N	12	14	26
- Mean +/- SD	49.8 +/- 17.9	48.6 +/- 15.2	49.1 +/-16.2
- p5, p25, p75, p95	26.2, 35.5, 64.6, 84.8	26.4, 37.8, 61.2, 77.8	26.4, 37.8, 63.6, 77.8
- Median	46.8	43.7	44.2
- Min, Max	26.2, 84.8	26.4, 77.8	26.2, 84.8
- 95% CI Mean	[38.5;61.2]	[39.8;57.3]	[42.6;55.7]
- 95% CI Median	[31.5;65.7]	[37.8;64.1]	[39.4;61.2]
Week 104: General Health			
- N	12	13	25
- Mean +/- SD	54.2 +/- 23.4	48.1 +/- 21.6	51.0 +/-22.2
- p5, p25, p75, p95	0.0, 50.0, 62.5, 100.0	25.0, 25.0, 50.0, 100.0	25.0, 50.0, 50.0, 100.0
- Median	50.0	50.0	50.0
- Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
- 95% CI Mean	[39.3;69.1]	[35.0;61.1]	[41.8;60.2]

	Treatment N=13	Control N=15	Total N=28
- 95% CI Median	[50.0;75.0]	[25.0;50.0]	[50.0;50.0]
Week 104: General Vision			
- N	12	13	25
- Mean +/- SD	43.3 +/- 16.7	33.8 +/- 17.1	38.4 +/-17.2
- p5, p25, p75, p95	20.0, 30.0, 60.0, 60.0	20.0, 20.0, 40.0, 60.0	20.0, 20.0, 60.0, 60.0
- Median	40.0	20.0	40.0
- Min, Max	20.0, 60.0	20.0, 60.0	20.0, 60.0
- 95% CI Mean	[32.7;53.9]	[23.5;44.2]	[31.3;45.5]
- 95% CI Median	[20.0;60.0]	[20.0;60.0]	[20.0;60.0]
Week 104: Ocular Pain			
- N	12	13	25
- Mean +/- SD	77.1 +/- 21.9	85.6 +/- 18.3	81.5 +/-20.1
- p5, p25, p75, p95	37.5, 56.3, 93.8, 100.0	37.5, 87.5, 100.0, 100.0	37.5, 75.0, 100.0, 100.0
- Median	87.5	87.5	87.5
- Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
- 95% CI Mean	[63.2;91.0]	[74.5;96.6]	[73.2;89.8]
- 95% CI Median	[50.0;100.0]	[75.0;100.0]	[75.0;100.0]
Week 104: Near Activities			
- N	12	13	25
- Mean +/- SD	36.8 +/- 26.2	30.8 +/- 17.8	33.7 +/-22.0
- p5, p25, p75, p95	0.0, 16.7, 58.3, 91.7	8.3, 16.7, 50.0, 58.3	8.3, 16.7, 50.0, 58.3
- Median	33.3	25.0	25.0
- Min, Max	0.0, 91.7	8.3, 58.3	0.0, 91.7
- 95% CI Mean	[20.1;53.5]	[20.0;41.5]	[24.6;42.7]
- 95% CI Median	[16.7;58.3]	[16.7;50.0]	[16.7;50.0]
Week 104: Distance Activities			
- N	12	13	25
- Mean +/- SD	34.7 +/- 28.6	32.4 +/- 20.4	33.5 +/-24.2
- p5, p25, p75, p95	0.0, 14.6, 56.3, 91.7	8.3, 16.7, 37.5, 75.0	8.3, 16.7, 50.0, 75.0
- Median	25.0	25.0	25.0
- Min, Max	0.0, 91.7	8.3, 75.0	0.0, 91.7
- 95% CI Mean	[16.6;52.9]	[20.0;44.7]	[23.5;43.5]
- 95% CI Median	[12.5;62.5]	[16.7;58.3]	[16.7;37.5]
Week 104: Vision Specific: Social Functioning			
- N	12	13	25
- Mean +/- SD	46.9 +/- 23.3	42.3 +/- 19.5	44.5 +/-21.1
- p5, p25, p75, p95	25.0, 25.0, 56.3, 100.0	12.5, 25.0, 62.5, 75.0	25.0, 25.0, 62.5, 75.0
- Median	43.8	37.5	37.5
- Min, Max	25.0, 100.0	12.5, 75.0	12.5, 100.0
- 95% CI Mean	[32.1;61.7]	[30.5;54.1]	[35.8;53.2]
- 95% CI Median	[25.0;62.5]	[25.0;62.5]	[25.0;50.0]
Week 104: Vision Specific: Mental Health			
- N	12	13	25
- Mean +/- SD	46.4 +/- 28.4	43.3 +/- 23.4	44.8 +/-25.4
- p5, p25, p75, p95	6.3, 25.0, 81.3, 87.5	0.0, 31.3, 56.3, 81.3	6.3, 25.0, 62.5, 81.3
- Median	34.4	50.0	43.8
- Min, Max	6.3, 87.5	0.0, 81.3	0.0, 87.5
- 95% CI Mean	[28.3;64.4]	[29.1;57.4]	[34.3;55.2]
- 95% CI Median	[25.0;81.3]	[25.0;62.5]	[31.3;56.3]
Week 104: Vision Specific: Role Difficulties			
- N	12	13	25
- Mean +/- SD	34.4 +/- 30.2	47.1 +/- 34.7	41.0 +/-32.6
- p5, p25, p75, p95	0.0, 0.0, 62.5, 75.0	0.0, 25.0, 75.0, 100.0	0.0, 0.0, 62.5, 87.5
- Median	31.3	62.5	37.5

	Treatment N=13	Control N=15	Total N=28
- Min, Max	0.0, 75.0	0.0, 100.0	0.0, 100.0
- 95% CI Mean	[15.2;53.6]	[26.2;68.1]	[27.6;54.4]
- 95% CI Median	[0.0;62.5]	[0.0;75.0]	[25.0;62.5]
Week 104: Vision Specific: Dependency			
- N	12	13	25
- Mean +/- SD	43.1 +/- 28.8	40.4 +/- 32.4	41.7 +/-30.1
- p5, p25, p75, p95	16.7, 20.8, 62.5, 100.0	0.0, 16.7, 66.7, 83.3	0.0, 16.7, 66.7, 83.3
- Median	29.2	33.3	33.3
- Min, Max	16.7, 100.0	0.0, 83.3	0.0, 100.0
- 95% CI Mean	[24.7;61.4]	[20.8;60.0]	[29.2;54.1]
- 95% CI Median	[16.7;75.0]	[8.3;83.3]	[16.7;66.7]
Week 104: Color Vision			
- N	12	12	24
- Mean +/- SD	70.8 +/- 29.8	68.8 +/- 28.5	69.8 +/-28.5
- p5, p25, p75, p95	25.0, 50.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0	25.0, 50.0, 100.0, 100.0
- Median	75.0	75.0	75.0
- Min, Max	25.0, 100.0	25.0, 100.0	25.0, 100.0
- 95% CI Mean	[51.9;89.8]	[50.7;86.8]	[57.7;81.8]
- 95% CI Median	[50.0;100.0]	[50.0;100.0]	[50.0;100.0]
Week 104: Peripheral Vision			
- N	12	13	25
- Mean +/- SD	62.5 +/- 29.2	59.6 +/- 33.1	61.0 +/-30.7
- p5, p25, p75, p95	25.0, 37.5, 87.5, 100.0	25.0, 25.0, 100.0, 100.0	25.0, 25.0, 100.0, 100.0
- Median	62.5	50.0	50.0
- Min, Max	25.0, 100.0	25.0, 100.0	25.0, 100.0
- 95% CI Mean	[44.0;81.0]	[39.6;79.6]	[48.3;73.7]
- 95% CI Median	[25.0;100.0]	[25.0;100.0]	[25.0;75.0]
Week 104: Composite Score			
- N	12	13	25
- Mean +/- SD	49.6 +/- 19.1	48.2 +/- 14.2	48.9 +/-16.4
- p5, p25, p75, p95	23.9, 35.6, 68.4, 78.7	24.1, 39.5, 57.3, 75.3	24.1, 37.2, 59.5, 75.3
- Median	43.4	45.3	45.3
- Min, Max	23.9, 78.7	24.1, 75.3	23.9, 78.7
- 95% CI Mean	[37.5;61.7]	[39.6;56.8]	[42.1;55.6]
- 95% CI Median	[35.2;70.2]	[37.2;59.5]	[38.2;58.2]

11.6 Mixed Effects Regression Analysis

Details of the model fit (mixed effects regression analysis) from the investigation of the influence of baseline value, group, and time after randomization on the visual acuity are shown in Table A 29.

Table A 29: Results from the Mixed effects Regression Analysis.

fixed effect	regression coefficient	95% confidence interval	p-value
intercept	1.006	0.490-1.523	0.001
group	0.039	-0.217-0.296	0.761
time	0.006	-0.002-0.015	0.129
va_base	-0.090	-0.747-0.567	0.786

The variable ‘group’ is the contrast MT group versus ST group. The variable ‘time’ is the change of the visual acuity per month. The variable ‘va_base’ is the baseline value of the visual acuity (logMAR).

11.7 Study Protocol

The study protocol is in a separate document.

11.8 Case Report Form

The case report form is in a separate document.

11.9 Statistical Analysis Plan

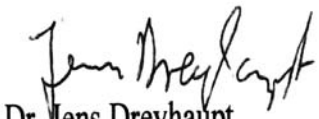
The statistical analysis plan is in a separate document.

11.10 Patients Data Listings

The listing of individual patients data is in a separate document.

Signatures

Heidelberg, 17.07.2007

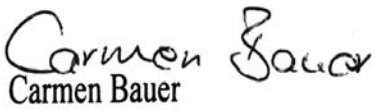


Dr. Jens Dreyhaupt

Heidelberg, 17.07.2007

Prof. Dr. Norbert Victor

Heidelberg, 17.07.2007



Carmen Bauer

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Appendix: