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# Early OCT Angiography Variations in Macular and Peripapillary Area after Uncomplicated Cataract Surgery and Correlation with Intraoperative Parameters

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**Abstract: Background**: We evaluated changes in both macular and peripapillary vascular parameters, evaluated by OCT angiography (OCTA), after uncomplicated cataract surgery, as well as the influence of effective phacoemulsification time (EPT) and cumulative dissipated energy (CDE). **Methods**: This is prospective study on 130 eyes of 65 individuals who underwent unilateral phacoemulsification, with fellow eyes data taken as control group. We collected cataract grading, EPT and CDE. Best corrected visual acuity (BCVA), superficial vessel density, deep vessel density, foveal avascular zone (FAZ) parameters and peripapillary capillary density were measured at baseline, one week and one month following surgery. **Results**: When compared to baseline, there was a significant increase in both superficial and deep foveal density at last follow up (from 42.9 ± 4.2 and 37.3 ± 7.4 to 45.6 ± 5.4 and 43.7 ± 9.0%, $p = 0.002$ and $p = 0.0001$, respectively). Both foveal avascular zone's area and perimeter showed a significant decrease compared to the preoperative value ($p < 0.05$). On the other hand, peripapillary vascular density showed a significant increase at week one (from 49.6 ± 2.7 to 51.4 ± 4.6%, $p = 0.01$), which returned to preoperative values at last follow up (49.3 ± 4.0%, $p = 0.95$). We found no significant differences when dividing the cohort for cataract severity. Moreover, no significant effect of the EPT and CDE on vascular changes were reported. **Conclusions**: We found a significant increase in the vascular parameters of the macular area after cataract surgery, while peripapillary vascular density only experienced a transient increase, suggesting an adaptative metabolic mechanism in response to increased light exposure after surgery.

**Keywords:** cataract surgery; ophthalmic surgery; vessel density; foveal avascular zone; optical coherence tomography angiography

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## 1. Introduction

Cataracts are the most avoidable cause of blindness, affecting globally roughly 20 million people [1]. This makes phacoemulsification the most common cataract surgery operation in ophthalmology. Although cataract surgery is performed on the anterior segment, its effects on the posterior segment have also been shown [2]. Variations in retinal thickness have previously been evaluated in ophthalmological literature, even after uncomplicated cataract surgery [3–6].

Optical coherence tomography (OCT) is one of the most innovative optical imaging modalities in recent decades. The original idea of OCT was to enable in-vivo optical biopsy, showing tissue microstructure with a resolution approaching that of histology without the need for tissue excision and processing [7,8]. Introduced at the beginning of the 1990s, this low-coherence interferometry allows for non-invasive evaluation of morphologic and functional tissue information. As of today, OCT is a fundamental instrument for ophthalmologists. This is largely due to resolution advancements of a factor of 10 to the submicron regime and an increase in imaging speed of more than 500,000 times to more than 5,000,000 A-scans per second, the latter of which was made possible by the cutting-edge swept source laser technologies [9,10]. Additionally, by implementing quasi-akinetic scanning, parallelization of OCT detection, such as line-field and full-field OCT, has further reduced the acquisition time. Moreover, recent reports presented a distortion-free OCT volumetric imaging using a dual-axis micro-electro-mechanical system (MEMS)-based portable imaging device. Using a Gabor-domain optical coherence microscope (GD-OCM), this system showed 2 μm axial and lateral resolutions over a field of view of $1 \times 1$ mm$^2$ [11].

After cataract surgery, the vast majority of investigations used OCT to identify changes in retinal thickness and the incidence of cystoid macular edema. Optical coherence tomography angiography (OCTA) has been introduced as a noninvasive imaging technique that displays the vascular density changes of the retina and choroid by recording the contrast of the movement in intravascular blood flow [12]. With OCTA, the microvascular network may be readily observed, which facilitates research into the development of retinal and choroidal illnesses and the monitoring of therapy efficacy [13].

With the advent of OCTA, the impact of cataract surgery on retinal vasculature and perfusion may be evaluated in greater detail. However, our present understanding of this area is somewhat restricted, since few research studies have been conducted. Despite this, alterations in vascular density and retinal perfusion have been recently documented after cataract surgery [14–19].

Our study's objective was to investigate early changes in retinal parameters measured by optical coherence tomography (OCTA) following uncomplicated cataract surgery, to understand whether it alters the microvascular structure of the macula and optic disc head. Additionally, we sought to assess if post-operative OCTA characteristics can be influenced by the stage of cataract progression, including the influence of effective phacoemulsification time (EPT) and cumulative dissipated energy (CDE) on vascularization parameters.

## 2. Materials and Methods

This prospective observational monocentric control-group study included pre-and post-operative data from 65 people who underwent elective unilateral cataract extraction performed between 1 February 2022 and 1 September 2022 at our ophthalmology unit in Fondazione Policlinico Universitario A. Gemelli—Rome. Data from patients who underwent phacoemulsification surgery with intraocular lens (IOL) implantation were retrieved and collected, along with data of the contralateral eye. This research adhered to the tenets of the Declaration of Helsinki and was approved by Catholic University of the Sacred Heart Ethical Committee in Rome, Italy. An informed and written consent was obtained from all enrolled patients.

The presence of a nuclear or cortical cataract with no concurrent intraocular illness and intraocular pressure (IOP) less than 21 mmHg were the inclusion criteria for the research. Exclusion criteria were: IOP greater than 21 mmHg, eyes with a posterior subscapularis or posterior polar cataract, axial length more than 26 mm or any aberrant intraocular findings. Moreover, patients who had had laser or photodynamic treatment in the past or who had glaucoma or other retinopathies (such as age-related macular degeneration, diabetic retinopathy, retinal vascular diseases, etc.) that may have altered the retinal microvascular network were also excluded. Patients who had a history of systemic illnesses including diabetes or inflammatory or cardiovascular conditions that could interfere with retinal vascular anomalies were also disqualified.

The final sample consisted of 130 eyes of 65 patients (35 men and 30 women). Patients varied in age from 45 to 85 years (mean age of $67.8 \pm 10.9$ years). The average spherical equivalent of preoperative refraction was 0.45 D for the eye undergoing cataract surgery and 0.39 for the fellow eye, and the average axial lengths 23.75 mm and 23.69 mm, respectively.

### *2.1. Examinations*

Prior to cataract surgery, all patients underwent standard examinations that included slit-lamp biomicroscopy, cataract grading, measurement of corrected distance visual acuity (CDVA) in Snellen chart, with successive conversion to the logarithm of the minimum angle of resolution (logMAR), measurement of intraocular pressure (IOP) with a Goldmann applanation tonometer and measurement of axial length (AL), anterior chamber depth and corneal keratometries with partial coherence interferometry (IOLMaster 700, Carl Zeiss-Meditec AG, Jena, Germany). The cataracts were graded at the biomicroscope using the 4 grading scales of the lens opacities classification system, version III (LOCS III): nuclear opalescence (NO, range 1–6), nuclear color (CO, range 0–6), cortical cataract (C, range 1–5) and posterior subcapsular cataract (P, range 1–5) [20].

In addition, we divided our sample into two groups based on the cataract severity grade in a post hoc analysis.

- Patients in Group 1 had less severe cataracts (C, NO, NC and P < 3).
- Patients in Group 2 had significant cataracts (C, NO, NC and P $\geq$ 3).

### *2.2. OCTA Protocol*

OCT and OCTA scans were performed using the Solix full-range OCT (Optovue Inc, Freemont, CA, USA), a new ultra-high-speed spectral domain device (version 2019 V1.0.0.317). Solix OCT runs at 120,000 A-scans per second and uses the split spectrum amplitude-decorrelation angiography (SSADA) algorithm. It has an Axial Resolution of 5 µm, a Lateral Resolution of 15 µm and a Transverse Resolution of 15 µm. Scan Depth can reach up to 3 mm in regular mode, and up to 6.25 mm in FullRange mode, while Scan Width ranges from 3 to 16 mm. Performing multiple B-scans in sequence, the software detects changes between each single scan which permits identification of the vasculature. For OCTA imaging, different scan sizes are available when analyzing retinal vascularization centered at the fovea (3 $\times$ 3 mm, 6.4 $\times$ 6.4 mm, 9 $\times$ 9 mm and 12 $\times$ 12 mm) or at the optic disc (4.5 $\times$ 4.5 mm).

Participant eyes underwent OCTA scans following pupil dilatation using 1% tropicamide solution both at baseline (preoperative visit, T0), seven days after surgery (T7) and thirty days after surgery (T30). Scans with a low-quality index ($\leq$7/10) (e.g., significant lens opacities, frequent eye blinks, excessive movement artifacts) were rejected. For every included eye, a minimum of three scans was performed at each follow-up. OCTA images were collected using the AngioVue software, to assess retinal vascularization in the whole macular region corresponding to a 6.4 $\times$ 6.4 mm field centered on the fovea. The software automatically evaluated the vessel density (VD) of the superficial and deep capillary plexuses (SCP, DCP). Moreover, the whole region was divided in superior and inferior halves. Inside the whole region, the scans also analyzed the fovea region that corresponded to the center ring (the area within the central 1-mm ring of the ETDRS grid), with the AngioVue software automatically calculating the foveal avascular zone (FAZ), which is a capillary-free region at the center of the macula. FAZ measurements are generated based on a pre-fixed retina slab (internal limiting membrane to outer plexiform layer +10µ). The collected parameters were: FAZ area in square millimeters over the 6.4 $\times$ 6.4 mm area in the full retinal plexus, the FAZ perimeter (in millimeters) and the retinal capillary flow density (FD). FD is calculated by dividing the number of vessels pixels by the total number of pixels, multiplied by 100%.

Moreover, 4.5 $\times$ 4.5 mm scans centered on the optic nerve head (ONH) were obtained: the in-built AngioVue Disc protocol was used to evaluate microvascular parameters. The software automatically calculated the values of capillary density (excluding large vessels) from the whole en face image (4.5 $\times$ 4.5 mm scan region) and the radial peripapillary capillary (RPC) vasculature, referred to a 0.75 mm wide elliptical annulus extending from the optic disc margin and successively divided in superior and inferior halves.

Each OCTA image underwent Motion Correction Technology (MCT) and 3D projection artifact removal to improve image quality. It is commonly understood that it takes at least a couple of seconds to acquire a 3D data volume at reasonable density with typical SD-OCT devices. Due to blinks and eye motion during scan acquisition, artifacts appear as distortion in the retinal blood vessel pattern and/or dark bands, as viewed in the en face image. Solix OCT system applies a proprietary software-based MCT to assess and correct motion in each volume. The system performs motion correction based on minimization of the overall difference between the two corrected volumes. The system generates the final 3D volume of an MCT scan based on the weighted average of the horizontal and vertical motion corrected volumes.

Finally, every scan was evaluated by two different retinal experts (M.M.C. and G.G.).

### 2.3. Surgical Technique

All cataract operations were done using the Centurion Vision System (Alcon Laboratories, Inc., Fort Worth, TX, USA) by a skilled surgeon (A.B.). The aforementioned "uncomplicated" surgery followed the steps of making a 2.2 mm clean corneal self-sealing incision, continuous capsulorhexis, hydrodissection, phacoemulsification, and irrigation/aspiration of the remnant lens cortex; these were carried out consecutively after a topical anesthetic. In the capsular bag, a foldable IOL (Alcon AcrySof® single-piece SA60WT, Alcon Laboratories Inc.) was implanted. The phacoemulsification machine's effective phacoemulsification time (EPT, measured in seconds) and phacoemulsification cumulative dissipated energy (CDE, expressed in micro-Joules, μJ) were recorded.

The postoperative fixed regimen included: Levofloxacin 0.5% eyedrops provided four times for ten days; Dexamethasone 0.1% and Netilmicin 0.3% eyedrops administered four times a day for seven days; and Diclofenac sodium 0.1% eyedrops administered four times a day for one month.

### 2.4. Statistical Analysis

GraphPad PRISM Software (Version 9.0; GraphPad, La Jolla, CA, USA) was used to analyze the resulting data. Shapiro-Wilk test was used to assess the normality of our sample, with $p$ value > 0.05 set to verify the null hypothesis. We conducted an ordinary one-way Analysis of Variance (ANOVA) and employed the Dunnett's multiple comparison test to evaluate the differences among retinal parameters in different follow ups. Furthermore, a Tukey test, computing confidence intervals, was used to compare the difference between each pair of means. Covariance analysis was conducted to assess the effect of the EPT and CDE on vascular changes. Finally, correlation and regression analyses were conducted for continuous variables. Quantitative values were expressed as mean ± SD and a $p$ value < 0.05 was considered statistically significant. A designated confidence interval (CI) of 95% was used.

## 3. Results

Sixty-five eyes of 65 patients with senile cataract fulfilled the assessment visits at baseline and after surgery. None of these patients underwent any surgical complication during and after surgery.

The mean corrected distance visual acuity (CDVA) before surgery was 0.32 ± 0.21 LogMAR (decimal equivalent 0.47, range 0.20–0.90). Median LOCS scale was N3, C2 and P0. There was a significant improvement in CDVA after cataract surgery, at each follow-up visit ($p$ < 0.001). Final CDVA was 0.0 LogMAR in all eyes (decimal equivalent 1.0), with a mean spherical equivalent of 0.10 D. In the fellow eyes, CDVA didn't show significant changes from baseline to last follow up visit (from 0.15 ± 0.14 to 0.17 ± 0.16 LogMAR, $p$ = 0.94). The mean EPT was 86.4 ± 18.7 s, and the mean CDE was 10.1 ± 3.5 μJ.

Demographic and main clinical outcomes are summarized in Table 1.

**Table 1.** Demographic characteristics of the study cohort and main intraoperative and functional outcomes.

| | **Data (Mean ± SD)** | |
|---|---|---|
| Age (years) | 67.8 ± 10.9 | |
| Sex (male/female) | 35/30 | |
| | Study Eye | Fellow Eye |
| Baseline CDVA (LogMAR) | 0.32 ± 0.21 | 0.15 ± 0.14 |
| Final CDVA (LogMAR) | 0.0 ± 0.0 | 0.17 ± 0.16 |
| Baseline SE (D) | 0.45 ± 0.24 | 0.36 ± 0.28 |
| Final SE (D) | 0.10 ± 0.05 | 0.36 ± 0.28 |
| Baseline IOP (mmHg) | 13.8 ± 3.9 | 14.2 ± 2.6 |
| One-week IOP (mmHg) | 11.3 ± 4.8 | 14.1 ± 2.9 |
| Final IOP (mmHg) | 13.2 ± 4.3 | 14.4 ± 3.0 |
| EPT (seconds) | 86.4 ± 18.7 | - |
| CDE (μJ) | 10.1 ± 3.5 | - |

CDVA = corrected distance visual acuity; SE = spherical equivalent; IOP = intraocular pressure; EPT = effective phacoemulsification time; CDE = cumulative dissipated energy.

### *3.1. Microvascular Variations*

Mean preoperative signal strengths were 8.4 ± 1.2 and 8.5 ± 1.1 for AngioVue 6.4 × 6.4 mm scan and for 4.5 × 4.5 AngioDisc scan, respectively. These results were comparable to the post operative period, for both T1 (8.6 ± 1.3 and 8.7 ± 1.2 for macula and disc, respectively) and T7 (8.7 ± 1.2 and 8.6 ± 1.3), with no statistically significant improvement ($p$ = 0.22 and $p$ = 0.33 when comparing pre-operative values to T1 and T7, respectively).

When compared to baseline, there was a significant increase in SCP vessel density at T30 (from 42.9 ± 4.2 to 45.6 ± 5.4, $p$ = 0.0001). On the other side, SCP vessel density at T7 showed a non-significant tendency to increase compared to T0 (43.4 ± 4.6, $p$ = 0.85). Similarly, DCP vessel density at T0 was 37.3 ± 7.4%, at T1 was 37.7 ± 10.4% ($p$ = 0.92), but showed a significant increase at T30 (43.7 ± 9.1%, $p$ = 0.0002) (Figure 1).

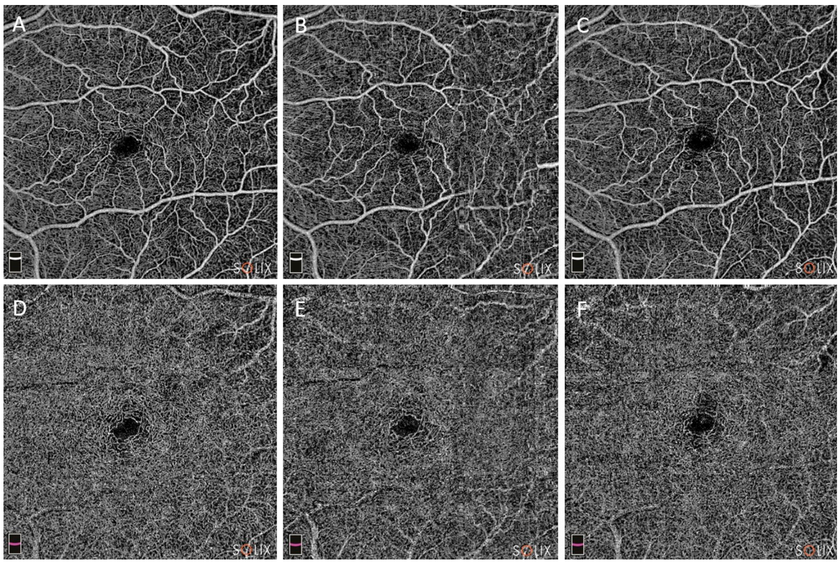


**Figure 1.** AngioVue Retina images of macular vascularization during the follow ups, in 6.4 × 6.4 mm scans. Upper images highlight the superficial capillary plexus (SCP): baseline (**A**), one week after cataract surgery (**B**) and one month after surgery (**C**). At last follow up, a significant increase in both whole image and foveal vascular density were reported (from 48.3% at T0, to 48.4 at T7, to 51.9% at T30). Similarly, the lower images show the deep capillary plexus (DCP) evolution at T0 (**D**), T7 (**E**) and T30 (**F**). DCP vascular density improved from 50.1% at T0, to 49.8% at T7 and finally to 54.0% at T30.

The FAZ parameters decreased significantly after cataract surgery. In particular, the mean preoperative FAZ area was 0.37 ± 0.22 mm$^2$ which significantly decreased to 0.26 ± 0.10 mm$^2$ at T7 ($p$ = 0.01) and to 0.27 ± 0.11 mm$^2$ at T30 ($p$ = 0.005). The mean preoperative FAZ perimeter was 2.53 ± 0.83 mm, which significantly decreased at both T7 and T30 (2.06 ± 0.48 mm and 2.04 ± 0.45 mm, $p$ = 0.003 and $p$ = 0.0008). The retinal capillary FD showed a non-significant variation at T7 when compared to T0 (from 40.0 ± 6.8 to 41.65 ± 6.5%, $p$ = 0.78), but significantly increased at T30 (44.9 ± 5.7, $p$ = 0.0016).

The analysis of optic nerve head microvascular parameters showed a significant increase in the whole image vessel density at T7 compared to the preoperative period (from 49.6 ± 2.7 to 51.4 ± 4.6%, $p$ = 0.001), but returned to preoperative values at T30 (49.3 ± 4.0%, $p$ = 0.95). Similarly, RCP vessel density showed a transient increase at T7 when compared to T0 (48.5 ± 6.2 vs. 45.6 ± 4.2%, $p$ = 0.001), but no significant changes were reported at T30 when compared to baseline values (44.8 ± 4.6 vs. 45.6 ± 4.2%, $p$ = 0.24) (Figure 2).

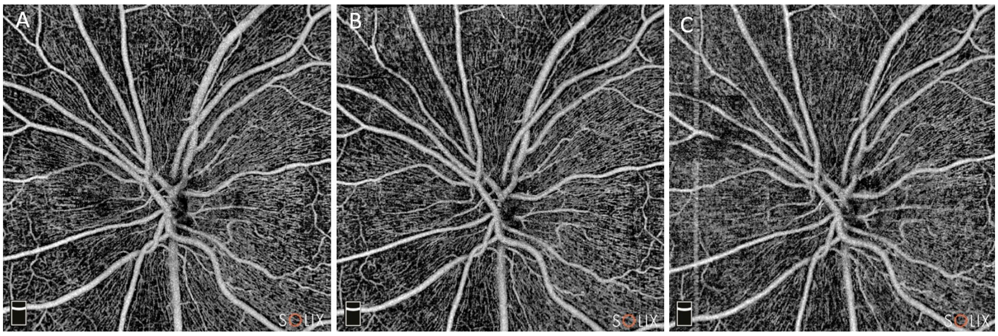


**Figure 2.** AngioVue Disc image of optic nerve head microvascularization during the follow ups: baseline (**A**), one week after cataract surgery (**B**) and one month after surgery (**C**). At last follow up, peripapillary vascular density is substantially unchanged when compared to baseline.

Figure 3 highlights the evolution of microvascular parameters through the follow ups.

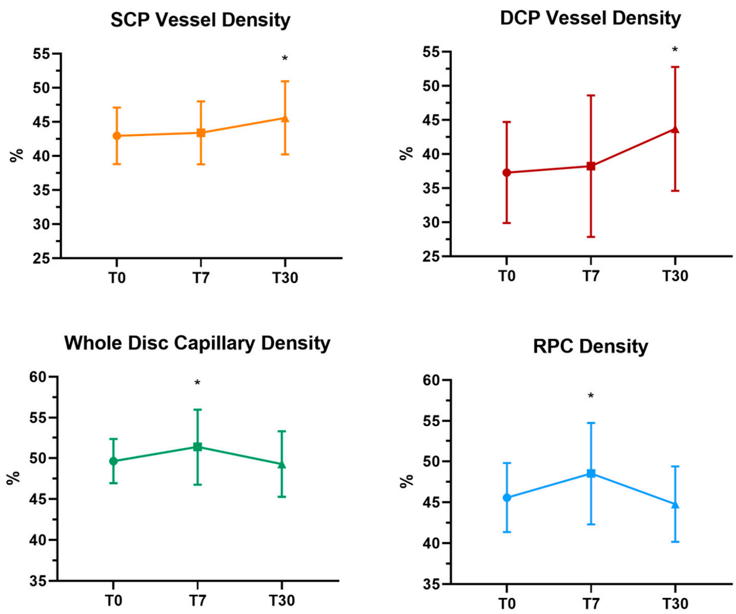


**Figure 3.** Column bar graphs showing the variation of study parameters at all follow ups (T0, T7, T30). Values are presented in mean ± standard deviation. SCP = superficial capillary plexus; DCP = deep capillary plexus; RPC = radial peripapillary capillary.

Fellow eyes did not show any significant changes at all follow ups considering every parameter. OCTA outcomes are all summarized in Table 2.

**Table 2.** Summary of all OCTA parameters in the treated eye at baseline (T0), one week after surgery (T7) and one month after surgery (T30). All parameters are presented in mean value ± standard deviation. In bold significant values.

| OCTA Parameters | | T0 | T7 | *p* | T30 | *p* |
|---|---|---|---|---|---|---|
| SCP | Superior (%) | 43.0 ± 3.6 | 43.2 ± 4.6 | 0.78 | 45.4 ± 5.3 | **0.0003** |
| | Inferior (%) | 42.9 ± 4.9 | 43.6 ± 4.6 | 0.58 | 45.8 ± 5.6 | **0.001** |
| | Whole (%) | 43.0 ± 4.2 | 43.4 ± 4.6 | 0.85 | 45.6 ± 5.4 | **0.0001** |
| DCP | Superior (%) | 36.6 ± 7.5 | 37.3 ± 7.4 | 0.48 | 42.9 ± 9.7 | **0.0005** |
| | Inferior (%) | 38.2 ± 8.3 | 38.2 ± 10.0 | 0.95 | 44.6 ± 8.6 | **0.003** |
| | Whole (%) | 37.3 ± 7.4 | 37.4 ± 11.1 | 0.92 | 43.7 ± 9.1 | **0.0002** |
| FAZ | Area (mm$^2$) | 0.38 ± 0.22 | 0.26 ± 0.10 | **0.01** | 0.27 ± 0.11 | **0.005** |
| | Perimeter (mm) | 2.53 ± 0.83 | 2.06 ± 0.48 | **0.003** | 2.04 ± 0.45 | **0.0008** |
| | FD (%) | 40.0 ± 6.8 | 41.65 ± 6.5 | 0.78 | 44.9 ± 5.7 | **0.0016** |
| ONH | Whole (%) | 49.6 ± 2.7 | 51.4 ± 4.6 | **0.001** | 49.3 ± 4.0 | 0.95 |
| | RPC (%) | 45.6 ± 4.2 | 48.5 ± 6.2 | **0.001** | 44.8 ± 4.6 | 0.24 |

SCP = superficial capillary plexus; DCP = deep capillary plexus; FAZ = foveal avascular zone; FD = flow density; ONH = optic nerve head; RPC = radial peripapillary capillary.

### *3.2. Subgroup Analysis*

Following the aforementioned criteria, Group 1 (less severe cataracts) included 35 eyes, while 30 eyes belonged to Group 2 (severe cataracts). Both groups showed significant visual improvement after surgery ($p$ = 0.002 and $p$ = 0.0001, respectively), with final CDVA being 0.0 LogMAR in all patients.

In Group 1, average EPT was 80.9 ± 21.0 s, compared to 92.8 ± 13.2 s in Group 2 ($p$ = 0.04). Furthermore, mean CDE values were 8.6 ± 3.4 and 11.5 ± 3.0 μJ in groups 1 and 2, respectively ($p$ = 0.02).

No significant differences between the two groups were reported preoperatively in retinal vascular parameters. In Group 1, SCP vessel density significantly increased at last follow up (from 43.0 ± 4.3 to 45.3 ± 4.5%, $p$ = 0.003). Similarly, DCP vessel density improved from baseline (38.1 ± 6.9%) to T30 (43.9 ± 8.8%) in a significant way ($p$ = 0.002). Both FAZ area (from 0.35 ± 0.20 to 0.22 ± 0.09 mm$^2$) and FAZ perimeter (from 2.23 ± 0.77 to 1.87 ± 0.44 mm) decreased significantly after cataract surgery at last follow up ($p$ = 0.001 and $p$ = 0.02, respectively). The retinal capillary FD significantly increased at T30 when compared to baseline (from 40.2 ± 6.2 to 43.2 ± 4.8, $p$ = 0.003). The optic nerve head vessel density in the whole 4.5 × 4.5 mm image did not show any significant increase at T30, compared to preoperative period (from 49.8 ± 2.0 to 48.8 ± 3.7%, $p$ = 0.35). Similarly, RCP vessel density changed from 45.1 ± 3.4 at T0 to 44.8 ± 4.5% at T30, in a non-significant way ($p$ = 0.68).

In Group 2, similar results were reported: both SCP and DCP vessel density showed a significant increase one month after surgery (from 43.0 ± 4.1 to 46.0 ± 6.3%, $p$ = 0.002, and from 36.5 ± 4.2 to 43.5 ± 9.6%, $p$ = 0.0001, respectively). FAZ parameters showed a significant improvement at the last follow up visit: FAZ area decreased from 0.40 ± 0.21 to 0.27 ± 0.08 mm$^2$ ($p$ = 0.001), whereas FAZ perimeter decreased from 2.59 ± 0.78 to 2.23 ± 0.38 mm. Furthermore, the retinal capillary FD increased at T30 when compared to baseline (from 38.9 ± 6.0 to 42.8 ± 5.8, $p$ = 0.01). On the other hand, both whole image and RCP vessel density at the optic disc showed no significant improvement at the end of the follow up period ($p$ = 0.18 and $p$ = 0.53, respectively).

Considering OCTA parameters at T30, contingency analysis showed no significant differences between Group 1 and Group 2 ($p$ > 0.05 for all comparisons).

### 3.3. Correlation of Microvascular Parameters to Intraoperative Parameters

Finally, regression analysis was conducted to evaluate the effect of intraoperative parameters (EPT and CDE) on vascular changes. Neither EPT nor CDE were linked with the variations of retinal vascular parameters, in either the macular or peripapillary region. The regression analyses are summarized in Table 3.

**Table 3.** Regression analysis to correlate EPT and CDE with variations SCP vessel density, DCP vessel density and ONH capillary density.

| Parameters | SCP Vessel Density | | DCP Vessel Density | | ONH Capillary Density | |
|---|---|---|---|---|---|---|
| | *Pearson r* | *p* | *Pearson r* | *p* | *Pearson r* | *p* |
| EPT | 0.12 | 0.34 | 0.19 | 0.15 | −0.18 | 0.33 |
| CDE | 0.22 | 0.09 | 0.24 | 0.08 | −0.21 | 0.11 |

EPT = effective phacoemulsification time; CDE = cumulative dissipated energy; SCP = superficial capillary plexus; DCP = deep capillary plexus; ONH = optic nerve head.

## 4. Discussion

In this work, we wanted to assess early postoperative retinal and peripapillary vascular alterations in eyes undergoing cataract surgery using a phacoemulsification approach.

A thorough retinal evaluation is an essential component of successful cataract surgery, even when the procedure is straightforward and without complications, since vascular alterations and pre-existing diseases of the retina have an impact on the final visual result [21]. Starting from this assumption, many investigations have been conducted to demonstrate possible retinal variations after phacoemulsification.

Over the last years, the OCT analysis gained importance and became fundamental in this setting. However, technological restrictions of the method must be taken into account when interpreting SD-OCT and OCTA data. For example, the quality of the scans is undoubtedly impacted by the cataract's existence. As a consequence, it is important to eliminate any potential bias brought on by the worse quality of presurgical scans. The manufacturer's guidelines state that the signal strength threshold (7/10) used in our investigation is likewise suitable for the analysis of SD-OCT and OCTA scans. Previous research has shown that worse OCT scan quality might influence measurement results, even if the signal intensity or quality index remained above the device manufacturer's recommended threshold. However, these publications often discussed the examination of the optic nerve, while there is evidence that the lesser quality of the macular cube scans has less of an impact on the measures [22,23]. The bias of poor-quality scans for OCT measures may thus be viewed as minimal in light of previous results as well as the high mean and median values of signal strength in our investigation [24,25].

For example, following cataract surgery, a temporary rise in central retinal thickness (CRT) was often seen, peaking at around 2–3 months after the procedure and then rapidly declining to lower or baseline levels [6,26,27]. A recent research study with a 12-months follow up reported that CRT was still greater at the end of the study period than it was at baseline [28]. Moreover, other studies have focused on vascular modifications induced by the procedure, thanks to the introduction of OCTA, which is able to evaluated both macro- and microcirculation of the retina [29]. However, with just a few studies available, there is a dearth of information on changes in OCTA parameters (vascular density and vascular perfusion) after cataract extraction [15–19]. In a research study on 55 eyes, Krizanovic et al. found that from the first week to the third month after cataract extraction, there was a consistent improvement in retinal arteries' length and area, which was particularly noticeable in the superficial vascular complex [14]. Comparably, a research study of 32 eyes by Zhao et al. revealed a significantly higher parafoveal and perifoveal vascular density 3 months after treatment, which was similar to the one reported by Feng et al. in a cohort of diabetic patients [16,18]. Interestingly, Li et al. observed that patients with low myopia (31 eyes) saw an improvement in vascular parameters 3 months after the operation, but patients with severe myopia experienced a deterioration (24 eyes) [17]. Another recent work showed how significant improvements in macular vascular parameters can be seen even 7 days after surgery [30].

In our group, the analysis of both SCP and DCP vessel density revealeded a significant increase one month after surgery, while at one-week follow up no variations in macular vascular parameters were reported. These results are consistent with the 1-month investigation of Zhou et al., who found a considerable improvement in macular and peripapillary vascular parameters, but the rise was seen only one week after surgery [19]. Moreover, similarly to the research conducted by Ozkan et al., we discovered that the DCP vessel density showed a more important variation than the SCP vessel density, even if both of them were significantly improved after surgery [31]. The DCP may be more prone to injury due to a number of factors, including distance from bigger arterioles, closeness to the outer retina's high metabolic requirement, and complicated vascular anatomic architecture. Base on this assumption, DCP may be more vulnerable to any perfusion defects and consequently more susceptible to changes in metabolic activity [32].

On the other hand, we found only a transient increase in peripapillary vascular parameters, which successively returned to baseline value at the end of the follow up. Similarly, despite the enhanced retinal vascularity, Ozkan reported no statistically significant changes in the peripapillary vessel density and optic nerve head area after surgery [31]. Conversely, in a research study on 24 eyes, the change in inside-disc values was not statistically significant in the first week but increased significantly in the first month [33]. Interestingly, the raise in peripapillary vessel density reported in our research coincided with a reduction in IOP found one week after surgery. Since numerous studies have shown how an alteration in IOP affects ocular hemodynamics, the postoperative transient drop in IOP may account for the rise in optic disc head vessel density [16,34]. Furthermore, peripapillary vascular parameters returned to baseline values when IOP stabilized one month after surgery.

Due to their repeatability and reliable findings in healthy eyes, the FAZ area measurements have been touted as a great noninvasive monitoring tool for retinal vascular alterations after cataract surgery [35]. In a recent study on 13 patients, the FAZ margin showed considerably improved distinguishability 1 week after surgery, although the FAZ area and circumference measures did not alter significantly [36]. Another research involving 32 participants showed that cataract surgery considerably reduced the FAZ area [16]. These results are consistent with our research, in which we reported a rapid and sustained reduction in both FAZ area and perimeter, along with a significant improvement in capillary flow density.

A few studies have been carried out regarding how phacoemulsification energy used during cataract surgery affects retinal metrics and vascular parameters. According to Kurt et al. there is a direct association between EPT and a rise in the thickness of the inner nuclear layer (INL) and ganglion cell layer (GCL) [37]. Similar to this, Golebiewska et al. reported increased retinal thickness and volume values with higher phaco power utilized during surgery, but not with longer phaco duration [38]. Other studies did not support the relationship between intraoperative variables (EPT, CDE) and postoperative retinal thickening [4,6]. Only the short-term research by Zhou et al. has examined the link between changes in vascular retinal parameters and the quantity of phaco energy utilized during the treatment to date. In that work, larger amounts of CDE utilized throughout the process were found to be associated with an increase in vascular density and perfusion density, despite not providing an explanation of this phenomenon's origin [19]. These results diverge from what we reported in our research, since a correlation between EPT or CDE parameters with retinal microvascular variations was not clear.

Several factors may have contributed to the increase in retinal vascular parameters after cataract surgery. First, as extensively documented in the literature, the increase in vascularization indexes could be caused by the inflammatory response brought on by the operation itself [39,40]. This surgically generated cytokine load may be a contributing factor to the enhanced vascular alterations of the retina. Interleukin 1-beta and chemokine ligand−2 were shown to be expressed from the neurosensory retina during cataract surgery, according to Xu et al., and may result in postoperative vascular dilation and blood-retinal barrier deterioration [41,42]. In our research, we divided the cohort into two groups, based on cataract hardness and severity. Intraoperative parameters showed significant differences between the two groups in both EPT and CDE: although higher energy and longer phacoemulsification times in harder cataracts could have caused higher rates of inflammation, no significant differences were found in retinal vascular changes during the considered follow up. Moreover, inflammation after cataract surgery is proven to peak within a few days of the procedure and then gradually subside over the course of two to three weeks [43]. Our research demonstrated that alterations in retinal characteristics appear after the very first postsurgical period, making the inflammatory hypothesis improbable. Furthermore, none of the eyes in our cohort showed any symptoms of persistent inflammation, such as cystoid macular edema, throughout the follow-up.

The second proposed mechanism is linked to a drop in intraocular pressure that has been seen during cataract surgery, which may enhance retinal perfusion and raise OCTA values [34,44]. Some studies of reported postoperative improvements in retinal arteries did not find a connection between a drop in intraocular pressure and an increase in ocular perfusion pressure [14,19]. In our research, the IOP drop found one week after surgery was linked to a increase in peripapillary vessel density but not in macular vessel density. Moreover, those findings were transient and disappeared at one-month follow up, alongside IOP stabilization.

The third mechanism indicates functional hyperemia, brought on by an increase in light exposure and improved retinal metabolism, as the carrier of vascular improvement after cataract surgery [45,46]. Since crystalline lenses may block between 18% and 40% of light, increased light exposure after its removal may determine increased retinal requests of metabolic mediators, such as oxygen and glucose [47]. As a consequence, molecular pathways induce the production of vasoactive mediators that cause vasodilation and hyperemia: these modifications should logically be reflected in a rise in OCTA parameters. Our findings show that the enhancement in retinal perfusion after cataract surgery progressively manifests after the initial post-surgical phase, suggesting the presence of retinal adaptation mechanisms to cope with the increased metabolic demands. Moreover, we found no changes in the peripapillary region, suggesting that the macular area is more susceptible to this phenomenon of increased metabolism due to its direct exposure to light.

One of the strengths of our research is that the use of one of the latest generation instruments (Solix full-range OCT, Optovue Inc., Freemont, CA, USA) helped us to minimize scan artifacts and possible bias due to low resolution. In particular, Motion Correction Technology (MCT) and 3D projection artifact removal were fundamental to evaluating slight changes, along with the possibility to analyze layer-by-layer vessel density to assess the effect of phacoemulsification surgery on retinal parameters.

This research has several limitations, starting from the small sample size, which may prevent the findings from being generalizable, even if this is one of the bigger cohorts in the literature and one of the few to have a control group. Second, the short follow up period may have limited the ability to establish the persistence of retinal changes. Finally, we only considered individuals without ocular or systemic illness. In fact, it is crucial to remember that, despite an improvement in vascular perfusion, increased light exposure can also cause angiogenesis, particularly in the category of age-related macular degeneration, becoming a risk rather than an advantage.

## 5. Conclusions

In conclusion, independently of the cataract severity grade and intraoperative parameters, the macular vessel density showed a significant increase one month after surgery, while optic nerve head vascularization was substantially unchanged. A larger sample size and longer follow-up times are necessary to fully explore the underlying processes of this adaptative mechanism.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Data can be obtained upon reasonable request to the corresponding author, M.M.C.

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## References

1. Pascolini, D.; Mariotti, S.P. Global estimates of visual impairment: 2010. *Br. J. Ophthalmol.* **2012**, *96*, 614–618. [CrossRef] [PubMed]
2. Azizi, B.; Wong, T.; Wan, J.; Singer, S.; Hudson, C. The impact of cataract on the quantitative, non-invasive assessment of retinal blood Flow. *Acta Ophthalmol.* **2012**, *90*, e9–e12. [CrossRef] [PubMed]
3. von Jagow, B.; Ohrloff, C.; Kohnen, T. Macular thickness after uneventful cataract surgery determined by optical coherence tomography. *Graefes. Arch. Clin. Exp. Ophthalmol.* **2007**, *245*, 1765–1771. [CrossRef] [PubMed]
4. Cagini, C.; Fiore, T.; Iaccheri, B.; Piccinelli, F.; Ricci, M.A.; Fruttini, D. Macular thickness measured by optical coherence tomography in a healthy population before and after uncomplicated cataract phacoemulsification surgery. *Curr. Eye Res.* **2009**, *34*, 1036–1041. [CrossRef]
5. Perente, I.; Utine, C.A.; Ozturker, C.; Cakir, M.; Kaya, V.; Eren, H.; Kapran, Z.; Yilmaz, O.F. Evaluation of macular changes after uncomplicated phacoemulsification surgery by optical coherence tomography. *Curr. Eye Res.* **2007**, *32*, 241–247. [CrossRef] [PubMed]
6. Gharbiya, M.; Cruciani, F.; Cuozzo, G.; Parisi, F.; Russo, P.; Abdolrahimzadeh, S. Macular thickness changes evaluated with spectral domain optical coherence tomography after uncomplicated phacoemulsification. *Eye* **2013**, *27*, 605–611. [CrossRef]
7. Huang, D.; Swanson, E.A.; Lin, C.P.; Schuman, J.S.; Stinson, W.G.; Chang, W.; Hee, M.R.; Flotte, T.; Gregory, K.; Puliafito, C.A. Optical coherence tomography. *Science* **1991**, *254*, 1178–1181. [CrossRef]
8. Fujimoto, J.G.; Brezinski, M.E.; Tearney, G.J.; Boppart, S.A.; Bouma, B.; Hee, M.R.; Southern, J.F.; Swanson, E.A. Optical biopsy and imaging using optical coherence tomography. *Nat. Med.* **1995**, *1*, 970–972. [CrossRef]
9. Drexler, W.; Liu, M.; Kumar, A.; Kamali, T.; Unterhuber, A.; Leitgeb, R.A. Optical coherence tomography today: Speed, contrast, and multimodality. *J. Biomed. Opt.* **2014**, *19*, 071412. [CrossRef]
10. Zysk, A.M.; Nguyen, F.T.; Oldenburg, A.L.; Marks, D.L.; Boppart, S.A. Optical coherence tomography: A review of clinical development from bench to bedside. *J. Biomed. Opt.* **2007**, *12*, 051403. [CrossRef]
11. Cogliati, A.; Canavesi, C.; Hayes, A.; Tankam, P.; Duma, V.-F.; Santhanam, A.; Thompson, K.P.; Rolland, J.P. MEMS-based handheld scanning probe with pre-shaped input signals for distortion-free images in Gabor-domain optical coherence microscopy. *Opt. Express* **2016**, *24*, 13365–13374. [CrossRef]
12. Sambhav, K.; Grover, S.; Chalam, K.V. The application of optical coherence tomography angiography in retinal diseases. *Surv. Ophthalmol.* **2017**, *62*, 838–866. [CrossRef]
13. Lains, I.; Wang, J.C.; Cui, Y.; Katz, R.; Vingopoulos, F.; Staurenghi, G.; Vavvas, D.G.; Miller, J.W.; Miller, J.B. Retinal applications of swept source optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). *Prog. Retin. Eye Res.* **2021**, *84*, 100951. [CrossRef]
14. Krizanovic, A.; Bjelos, M.; Busic, M.; Elabjer, B.K.; Rak, B.; Vukojevic, N. Macular perfusion analysed by optical coherence tomography angiography after uncomplicated phacoemulsification: Benefits beyond restoring vision. *BMC Ophthalmol.* **2021**, *21*, 71. [CrossRef]
15. Pilotto, E.; Leonardi, F.; Stefanon, G.; Longhin, E.; Torresin, T.; Deganello, D.; Cavarzeran, F.; Miglionico, G.; Parrozzani, R.; Midena, E. Early retinal and choroidal OCT and OCT angiography signs of inflammation after uncomplicated cataract surgery. *Br. J. Ophthalmol.* **2019**, *103*, 1001–1007. [CrossRef] [PubMed]
16. Zhao, Z.; Wen, W.; Jiang, C.; Lu, Y. Changes in macular vasculature after uncomplicated phacoemulsification surgery: Optical coherence tomography angiography study. *J. Cataract Refract. Surg.* **2018**, *44*, 453–458. [CrossRef] [PubMed]
17. Li, T.; Guadie, A.; Feng, L.; Fan, J.; Jiang, Z.; Liu, F. Influence of cataract surgery on macular vascular density in patients with myopia using optical coherence tomography angiography. *Exp. Ther. Med.* **2020**, *20*, 258. [CrossRef] [PubMed]
18. Feng, L.; Azhati, G.; Li, T.; Liu, F. Macular Vascular Density Changes following Cataract Surgery in Diabetic Patients: An Optical Coherence Tomography Angiography Study. *J. Ophthalmol.* **2021**, *2021*, 6641944. [CrossRef]

19. Zhou, Y.; Zhou, M.; Wang, Y.; Ben, S.; Gao, M.; Zhang, S.; Liu, H.; Sun, X. Short-Term Changes in Retinal Vasculature and Layer Thickness after Phacoemulsification Surgery. *Curr. Eye Res.* **2020**, *45*, 31–37. [CrossRef]
20. Chylack, L.T., Jr.; Leske, M.C.; Sperduto, R.; Khu, P.; McCarthy, D. Lens Opacities Classification System. *Arch. Ophthalmol.* **1988**, *106*, 330–334. [CrossRef]
21. McKeague, M.; Sharma, P.; Ho, A.C. Evaluation of the macula prior to cataract surgery. *Curr. Opin. Ophthalmol.* **2018**, *29*, 4–8. [CrossRef] [PubMed]
22. Rao, H.L.; Addepalli, U.K.; Yadav, R.K.; Senthil, S.; Choudhari, N.S.; Garudadri, C.S. Effect of scan quality on diagnostic accuracy of spectral-domain optical coherence tomography in glaucoma. *Am. J. Ophthalmol.* **2014**, *157*, 719–727.e1. [CrossRef] [PubMed]
23. Na, J.H.; Sung, K.R.; Lee, Y. Factors associated with the signal strengths obtained by spectral domain optical coherence tomography. *Korean J. Ophthalmol.* **2012**, *26*, 169–173. [CrossRef] [PubMed]
24. Yu, J.; Camino, A.; Liu, L.; Zhang, X.; Wang, J.; Gao, S.S.; Jia, Y.; Huang, D. Signal strength reduction effects in OCT angiography. *Ophthalmol. Retin.* **2019**, *3*, 835–842. [CrossRef]
25. Lujan, B.J.; Calhoun, C.T.; Glassman, A.R.; Googe, J.M.; Jampol, L.M.; Melia, M.; Schlossman, D.K.; Sun, J.K. Optical coherence tomography angiography quality across three multicenter clinical studies of diabetic retinopathy. *Transl. Vis. Sci. Technol.* **2021**, *10*, 2. [CrossRef] [PubMed]
26. Jiang, H.; Li, Z.; Sun, R.; Liu, D.; Liu, N. Subfoveal choroidal and macular thickness changes after phacoemulsification using enhanced depth imaging optical coherence tomography. *Ophthalmic Res.* **2018**, *60*, 243–249. [CrossRef]
27. Giansanti, F.; Bitossi, A.; Giacomelli, G.; Virgili, G.; Pieretti, G.; Giuntoli, M.; Abbruzzese, G.; Menchini, U. Evaluation of macular thickness after uncomplicated cataract surgery using optical coherence tomography. *Eur. J. Ophthalmol.* **2013**, *23*, 751–756. [CrossRef]
28. Gawecki, M.; Pradzynska, N.; Karska-Basta, I. Long-Term Variations in Retinal Parameters after Uncomplicated Cataract Surgery. *J. Clin. Med.* **2022**, *11*, 3426. [CrossRef] [PubMed]
29. Wei, E.; Jia, Y.; Tan, O.; Potsaid, B.; Liu, J.J.; Choi, W.; Fujimoto, J.G.; Huang, D. Parafoveal retinal vascular response to pattern visual stimulation assessed with OCT angiography. *PLoS ONE* **2013**, *8*, e81343. [CrossRef]
30. Baldascino, A.; Ripa, M.; Carla, M.M.; Caporossi, T.; Grieco, G.; Gambini, G.; De Vico, U.; Raguso, G.; Kilian, R.; Rizzo, C.; et al. Optical Coherence Tomography Angiography to Estimate Early Retinal Blood Flow Changes after Uncomplicated Cataract Surgery. *Vision* **2022**, *6*, 38. [CrossRef]
31. Ozkan, B.; Ciloglu, E. Evaluation of the Effect of Uncomplicated Cataract Surgery on Retina and Optic Disc: Optical Coherence Tomography Angiography Study. *Korean J. Ophthalmol.* **2022**, *36*, 287–295. [CrossRef] [PubMed]
32. Nakahara, T.; Hoshino, M.; Hoshino, S.; Mori, A.; Sakamoto, K.; Ishii, K. Structural and functional changes in retinal vasculature induced by retinal ischemia-reperfusion in rats. *Exp. Eye Res.* **2015**, *135*, 134–145. [CrossRef] [PubMed]
33. Karabulut, M.; Karabulut, S.; Sul, S.; Karalezli, A. Optic nerve head microvascular changes after phacoemulsification surgery. *Graefes. Arch. Clin. Exp. Ophthalmol.* **2019**, *257*, 2729–2733. [CrossRef] [PubMed]
34. Hilton, E.J.; Hosking, S.L.; Gherghel, D.; Embleton, S.; Cunliffe, I.A. Beneficial effects of small-incision cataract surgery in patients demonstrating reduced ocular blood flow characteristics. *Eye* **2005**, *19*, 670–675. [CrossRef]
35. Carpineto, P.; Mastropasqua, R.; Marchini, G.; Toto, L.; Di Nicola, M.; Di Antonio, L. Reproducibility and repeatability of foveal avascular zone measurements in healthy subjects by optical coherence tomography angiography. *Br. J. Ophthalmol.* **2016**, *100*, 671–676. [CrossRef]
36. Yu, S.; Frueh, B.E.; Steinmair, D.; Ebneter, A.; Wolf, S.; Zinkernagel, M.S.; Munk, M.R. Cataract significantly influences quantitative measurements on swept-source optical coherence tomography angiography imaging. *PLoS ONE* **2018**, *13*, e0204501. [CrossRef]
37. Kurt, A.; Kilic, R. The Effects of Uncomplicated Cataract Surgery on Retinal Layer Thickness. *J. Ophthalmol.* **2018**, *2018*, 7218639. [CrossRef]
38. Gołebiewska, J.; Kęcik, D.; Turczyńska, M.; Moneta-Wielgoś, J.; Kopacz, D.; Pihowicz-Bakoń, K. Evaluation of macular thickness after uneventful phacoemulsification in selected patient populations using optical coherence tomography. *Klin. Ocz.* **2014**, *116*, 242–247.
39. Wielders, L.H.P.; Schouten, J.; Winkens, B.; van den Biggelaar, F.; Veldhuizen, C.A.; Findl, O.; Murta, J.C.N.; Goslings, W.R.O.; Tassignon, M.J.; Joosse, M.V.; et al. European multicenter trial of the prevention of cystoid macular edema after cataract surgery in nondiabetics: ESCRS PREMED study report 1. *J. Cataract Refract. Surg.* **2018**, *44*, 429–439. [CrossRef]
40. Kessel, L.; Tendal, B.; Jorgensen, K.J.; Erngaard, D.; Flesner, P.; Andresen, J.L.; Hjortdal, J. Post-cataract prevention of inflammation and macular edema by steroid and nonsteroidal anti-inflammatory eye drops: A systematic review. *Ophthalmology* **2014**, *121*, 1915–1924. [CrossRef]
41. Xu, H.; Chen, M.; Forrester, J.V.; Lois, N. Cataract surgery induces retinal pro-inflammatory gene expression and protein secretion. *Investig. Ophthalmol. Vis. Sci.* **2011**, *52*, 249–255. [CrossRef] [PubMed]
42. Ambati, J.; Anand, A.; Fernandez, S.; Sakurai, E.; Lynn, B.C.; Kuziel, W.A.; Rollins, B.J.; Ambati, B.K. An animal model of age-related macular degeneration in senescent Ccl-2-or Ccr-2-deficient mice. *Nat. Med.* **2003**, *9*, 1390–1397. [CrossRef]
43. Taravati, P.; Lam, D.L.; Leveque, T.; Van Gelder, R.N. Postcataract surgical inflammation. *Curr. Opin. Ophthalmol.* **2012**, *23*, 12–18. [CrossRef]
44. Melancia, D.; Abegao Pinto, L.; Marques-Neves, C. Cataract surgery and intraocular pressure. *Ophthalmic Res.* **2015**, *53*, 141–148. [CrossRef] [PubMed]

45. Kur, J.; Newman, E.A.; Chan-Ling, T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. *Prog. Retin. Eye Res.* **2012**, *31*, 377–406. [CrossRef] [PubMed]
46. Attwell, D.; Buchan, A.M.; Charpak, S.; Lauritzen, M.; Macvicar, B.A.; Newman, E.A. Glial and neuronal control of brain blood flow. *Nature* **2010**, *468*, 232–243. [CrossRef] [PubMed]
47. Artigas, J.M.; Felipe, A.; Navea, A.; Fandino, A.; Artigas, C. Spectral transmission of the human crystalline lens in adult and elderly persons: Color and total transmission of visible light. *Investig. Ophthalmol. Vis. Sci.* **2012**, *53*, 4076–4084. [CrossRef]