

The Impact of Cataract Surgery with Low and High Fluidic Settings on Different Retinal Segments

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ABSTRACT

Purpose: To evaluate the effects of cataract surgery with high and low fluidic parameters on individuals retinal thicknesses in early postoperative period.

Material and Methods: The study included 64 eyes of 64 patients who underwent uncomplicated phacoemulsification surgery for senile cataract. The patients were randomized to phacoemulsification with low (32 eyes) and high fluidic parameters (32 eyes). In both groups, the amount of balanced salt solution used (ABS), cumulative dissipated energy (CDE) and surgical time were recorded. Macular segmentation analysis in the foveal and parafoveal area was performed with spectral-domain optical coherence tomography (OCT) before surgery and on days 7 and 30 after surgery, and the OCT Fast Macular Thickness program was used to measure the thickness of individual retinal layers in both groups.

Results: The mean age of the patients in the low and high fluidic groups were 61.8±5.4 and 60.4±6.7 years, respectively. The mean CDE and surgical time were significantly higher in the group using low fluidic parameters, while the mean ABS was significantly higher in the high fluidic group. On day 7 after surgery, there was a significant increase in the thickness of the parafoveal inner nuclear layer in the patients group who underwent surgery at high fluidic parameters, while no significant difference was observed in the low fluidic groups. On the 30th day after surgery, a significant increase was observed in the thickness of the parafoveal outer nuclear and inner nuclear layers in both groups, and the change in this layers was significantly higher in the high fluidic group.

Conclusion: This study shows that the increased intraocular pressure during surgery due to high bottle level may also have an effect in the pathophysiology of inner retinal layer thickening in addition to the role of surgical induced inflammation.

Keywords: Phacoemulsification, low and high flow parameters, macular segmentation.

INTRODUCTION

The predictability of outcomes and safety has been improved in the cataract surgery owing to advances in phaco power modes, variable vacuum level and aspiration flow rates by improvements in phacoemulsification technology.¹⁻³ The fluid fluctuations in anterior segment was reduced during cataract surgery by these advances, allowing safe and controlled surgery. Moreover, owing to improved surgical safety, varying vacuum levels and aspiration flow rates have been introduced into surgery while using phacoemulsification techniques with varying energy modes.⁴ Surgeons have adopted several surgical approaches which may differ with low or high vacuum level, aspiration rate and bottle height at continuous or

interrupted energy modes. It is aimed to decrease surgical time and minimize duration and amount of ultrasound energy dissipated within eye in surgical procedures using high fluidic parameters (high vacuum, aspiration rate and bottle height). In low fluidic parameters, it was aimed to reduce trauma resulting from fluid turbulence and improve safety for surrounding tissues.

Although many studies have investigated safety and effects of cataract surgery using different fluid dynamics on anterior segment, there is limited number of studies about effects on retina.⁵⁻⁷ The short- and long-term effects of cataract surgery using high and low fluidic parameters on retina are unclear. The advances in optical coherence tomography (OCT) technology allows segmentation and

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measurement of thickness in individual retinal layers by Spectralis OCT (Heidelberg Engineering, Inc., Heidelberg, Germany) using certain software.⁸ This method allows observing changes in detailed histological sections of retina after cataract surgery performed using different fluid dynamics. Therefore, it was aimed to evaluate effects of cataract surgery performed using low and high fluidic parameters on retina at early postoperative period.

MATERIALS AND METHODS

This prospective, clinical study was conducted at Ophthalmology department of Kütahya Health Sciences University, Medicine School between February, 2019 and April, 2020. The study was approved by Committee on Education and Planning. The study was conducted in accordance to tenets of Helsinki Declaration. All participants gave written informed consent. The study included 64 eyes of 64 patients who underwent uncomplicated phacoemulsification surgery for senile cataract. In all patients, a comprehensive ophthalmological examination was performed, including corrected visual acuity (VA) measurement by Snellen chart, cataract grading using slit-lamp examination (LCOS II classification, Grade 1-4), dilated fundus examination, intraocular pressure (IOP) measurement using pneumotonometer, auto-refractometry measurement, axial length measurement, intraocular lens

power calculation and spectral domain-optical coherence tomography (SD-OCT) imaging. The VA measurement, IOP measurement and SD-OCT imaging were repeated on day 7 and 30 after surgery. The patients with previous ocular surgery; those with uveitis or glaucoma; those with any corneal or retinal disease (diabetic retinopathy, macular degeneration, epiretinal membrane); those with traumatic or dense cataract which may hamper OCT imaging; those with anterior chamber depth <2,5 mm, diameter <5 mm and axial length >25; those experienced complication during surgery (posterior capsule injury, vitreous loss, zonule damage); those with spherical and cylindrical refractive error >3 diopters; and those with poor SD-OCT signal quality (<20) at preoperative period were excluded. In addition, patients with uncontrolled systemic disease, connective tissue disorders and diabetes mellitus as well as those with history of previous photocoagulation or intravitreal injection therapy were also excluded.

The patients included were randomized to undergo phacoemulsification surgery with low (group 1) and high (group 2) fluidic parameters. In both groups, torsional ultrasound power was set as continuous ultrasound mode 40% (range: 40-80%; Centurion® Vision System; Alcon Laboratories, Fort Worth, TX, USA) and surgical parameters are presented in Table 1. All surgical procedures were performed under topical anesthesia (Alcain, Proparacaine

Table 1: Surgical parameters and postoperative data

| | Low fluidic group | High fluidic group | <i>p</i> * |
|--|-------------------|--------------------|------------|
| Pre-phaco | | | |
| Bottle level (cm) | 60 | 110 | |
| Aspiration (mL/min) | 21 | 28 | |
| Vacuum (mmHg) | 80 | 80 | |
| Phaco (chop) | | | |
| Bottle level (cm) | 60 | 110 | |
| Aspiration (mL/min) | 25 | 32 | |
| Vacuum (mmHg) | ≤300 | 450 | |
| Irrigation/aspiration | | | |
| Bottle level (cm) | 60 | 110 | |
| Aspiration (mL/min) | 25 | 32 | |
| Vacuum (mmHg) | 350 | 450 | |
| CDE | 15.6±5.7 | 9.6±4.3 | <0.001 |
| ABS | 82.9±14.2 | 98.6±19.4 | <0.001 |
| Surgical time | 9.3±1.6 | 7.4±1.8 | 0.004 |
| *:Independent t test, Phaco: Phacoemulsification, Pre-phaco: Pre-phacoemulsification, CDE: cumulative dissipated energy , ABS: amount of balances salt solution used | | | |

hydrochloride 0.5%) by same experienced surgeon (FÖ) using similar techniques. Phacoemulsification was performed by phaco-chop technique using 0.9 mm mini-flared ABS (aspiration bypass system, Alcon, Inc.,) 45°C Kelman tip in torsional mode. In all patients, prophylactic 0.5% moxifloxacin (Vigamox®) was given via intracameral route at the end of surgery. In both groups, all patients were prescribed topical corticosteroid (4x1 for 3 weeks; 1.5% prednisolone acetate; Pred Forte, Allergan) and antibiotic (4x1 for 3 weeks) Vigamox, Alcon). In both groups, the amount of balanced salt solution used (ABS) and cumulative dissipated energy (CDE) were recorded at the end of surgery. Corneal time and time from corneal incision to antibiotic prophylaxis were also recorded.

The SD-OCT Fast Macular Thickness software was used for macular segment analysis and measurement of thickness of individual retinal layers before and after surgery. All images were captured between 09:00 AM and 10:00 AM by an experienced ophthalmologist (OA) and automated OCT segmentation (Spectralis version 6.0.0.2 Heidelberg Engineering, Inc) was confirmed by an experienced ophthalmologist (OA) blinded to groups. After capturing OCT images, all images were checked to ensure presence of marked foveal pit in the center of scan. In case of misalignment, retinal segmentation was performed following manual alignment. Retinal segmentation analysis stratifies retinal thickness into 7 layers in a single, horizontal foveal scan in an automated manner and calculates mean thickness for each layer. The mean thicknesses of retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL) and retinal pigment epithelium (RPE) were analyzed within 1-3 mm ETDRS sub-areas. The circular area 1 mm from center of ETDRS grid was termed as foveal region while the circular area 1 to 3 mm from ETDRS grid was defined as parafoveal region.

Statistical analysis

All data were analyzed using SPSS (Statistical Package for Social Sciences) for Windows version 21.0 (SPSS Inc, Chicago, IL). Quantitative variables are presented as mean \pm standard deviation while qualitative variables are presented as frequency and percent. The normality was assessed using Shapiro-Wilk test. Independent samples t test or chi-square test was used to compare variables and primary clinical characteristics between groups. The changes in retinal layer from baseline to postoperative days 1 and 7 were analyzed using paired t test. A p value $<$ 0.05 was considered as statistically significant.

RESULTS

In the study, we analyzed 32 eyes of 32 patients underwent cataract surgery using low surgical parameters and 32 eyes of 32 patients underwent surgery using high surgical parameters. , there was 32 patients). The mean age was 61.8 ± 5.4 (56-72) years in the low fluidic parameter group (17 men; 15 women) while it was 60.4 ± 6.7 (55-71) years in the high fluidic parameter group (19 men, 13 women). There was no significant difference in age, gender and ocular parameters between groups (Table 2).

Table 1 summarizes mean ABS, CDE and surgical times in both groups. Mean CDE and surgical time were significantly higher in the low fluidic parameter group while mean ABS was significantly higher in the high fluidic parameter group.

Table 3-4 presents thicknesses of different retinal segments at preoperative period and early postoperative period. On postoperative day 7, a significant increase was observed in parafoveal INL thickness in the patients underwent cataract surgery with high fluidic parameters while no significant difference was observed in the patients underwent cataract surgery with low fluidic parameters. On postoperative day 30, a significant increase was observed in parafoveal ONL,

Table 2: Demographic characteristics and ocular parameters before surgery

| | Low fluidic group | High fluidic group | p |
|--|-------------------|--------------------|---------|
| Age | 61.8 \pm 5.4 | 60.4 \pm 6.7 | 0.396 |
| Gender (male/female) | 17/15 | 19/13 | 0.356** |
| Axial length (mm) | 23.3 \pm 0.9 | 22.9 \pm 1.1 | 0.467 |
| Cataract (LOCS III) | 3.0 \pm 0.8 | 3.1 \pm 0.9 | 0.541 |
| CCT (μ m) | 541.6 \pm 36.8 | 538.6 \pm 41.3 | 0.216 |
| ACD (mm) | 3.2 \pm 0.3 | 3.1 \pm 0.4 | 0.635 |
| ** : Chi-square test, * :Independent t test, LOCS III: Lens Opacity Classification System, CCT: Central corneal thickness, ACD: Anterior chamber depth | | | |

Table 3: Preoperative foveal and parafoveal retinal thicknesses

| | Low fluidic group | High fluidic group | p* |
|-------------|-------------------|--------------------|-------|
| TMT | | | |
| Foveal | 273.2±23.1 | 274.1±24.5 | >0.05 |
| Parafoveal | 332.3±31.0 | 334.7±28.6 | >0.05 |
| RPE | | | |
| Foveal | 16.3±3.4 | 15.9±3.8 | >0.05 |
| Parafoveal | 14.6±1.9 | 15.1±2.3 | >0.05 |
| ONL | | | |
| Foveal | 90.2±12.1 | 91.5±13.6 | >0.05 |
| Parafoveal | 72.2±8.7 | 73.1±9.2 | >0.05 |
| OPL | | | |
| Foveal | 29.3±6.3 | 27.6±7.3 | >0.05 |
| Parafoveal | 32.1±7.0 | 31.0±6.4 | >0.05 |
| INL | | | |
| Foveal | 26.8±5.0 | 27.3±6.1 | >0.05 |
| Parafoveal | 39.6±4.7 | 41.2±3.5 | >0.05 |
| IPL | | | |
| Foveal | 21.5±4.5 | 20.4±5.2 | >0.05 |
| Parafoveal | 39.5±5.9 | 38.6±5.4 | >0.05 |
| GCL | | | |
| Foveal | 18.1±4.8 | 17.1±4.3 | >0.05 |
| Parafoveal | 49.1±9.5 | 49.6±9.8 | >0.05 |
| RNFL | | | |
| Foveal | 13.2±2.3 | 15.2±2.8 | >0.05 |
| Parafoveal | 21.1±5.3 | 21.4±5.6 | >0.05 |

*:Independent t test, TMT:Total macular thickness, RPE: Retina pigment epithelium thickness, ONL: Outer nuclear layer thickness, OPL: Outer plexiform layer thickness; INL: Inner nuclearr layer thickness, IPL: Inner plexiform layr thickness, GCL: Ganglion cell layer thickness, RNFL: Retina nerve fiber layer thickness

OPL and INL thicknesses in both groups; in addition, the extent of increase was greater in the high fluidic parameter group. A linear regression analysis was performed to determine prognostic factor related to increased parafoveal INL and DNL on postoperative days 7 and 30. However, no significant effect of surgical parameters, CDE and surgical time on retinal layer thicknesses was observed ($p>0.05$).

When visual acuity was considered, in the low fluidic parameter group, the mean corrected visual acuity by Snellen chart was 0.12 ± 0.08 , 0.88 ± 0.10 and 0.91 ± 0.08 , respectively. In the high fluidic parameter group, the mean VA was 0.11 ± 0.09 , 0.89 ± 0.12 and 0.9 ± 0.05 at baseline, on postoperative day 7 and day 30, respectively. No significant difference was observed in VA on postoperative day 7 and day 30 in between groups ($p=0.437$, $p=0.511$). Mean IOP at baseline was 15.5 ± 1.7 and 16.2 ± 2.1 mmHg while mean

IOP was 14.7 ± 2.2 and 14.5 ± 2.0 on postoperative day 7 and 15.8 ± 2.3 and 15.4 ± 2.1 mmHg on postoperative day 30 in low and high fluidic parameter groups, respectively. No significant difference was observed in IOP on postoperative day 7 and 30 between groups ($p>0.05$).

DISCUSSION

Today, owing to advances in phacoemulsification technology, safe surgical procedures with shorter duration using high fluidic parameters in cataract surgery are being commonly preferred by surgeons. However, some surgeons prefer more controlled, low fluidic parameters to reduce turbulent flow-related potential trauma caused by high fluidic parameters.⁴ Although many studies have investigated safety and effects of cataract surgery using different fluid dynamics on anterior segment, there

Table 4: Foveal and parafoveal retinal thicknesses on postoperative day 7 and day 30

| | Low fluidic group | | | | High fluidic group | | | | p ^{&} | |
|-------------|-------------------|-------|------------|-------------|--------------------|-------------|------------|--------------|--------------------|-------------|
| | Day 7 | p* | Day 30 | p** | Day 7 | p* | Day 30 | p** | Day 7 | Day 30 |
| TMT | | | | | | | | | | |
| Foveal | 275.4±25.8 | >0.05 | 276.5±28.7 | >0.05 | 276.8±28.3 | >0.05 | 280.3±36.4 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 334.7±32.5 | >0.05 | 341.5±35.3 | 0.03 | 337.1±33.6 | >0.05 | 349.0±39.1 | 0.02 | >0.05 | >0.05 |
| RPE | | | | | | | | | | |
| Foveal | 16.8±3.1 | >0.05 | 16.7±3.2 | >0.05 | 16.0±3.7 | >0.05 | 15.8±3.4 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 14.9±1.8 | >0.05 | 14.8±1.7 | >0.05 | 15.3±2.4 | >0.05 | 15.2±2.5 | >0.05 | >0.05 | >0.05 |
| ONL | | | | | | | | | | |
| Foveal | 91.5±12.8 | >0.05 | 92.8±11.9 | >0.05 | 92.7±13.1 | >0.05 | 95.3±13.5 | 0.01 | >0.05 | 0.02 |
| Parafoveal | 73.4±9.2 | >0.05 | 77.5±8.9 | 0.01 | 74.3±9.5 | >0.05 | 81.4±9.6 | 0.001 | >0.05 | 0.01 |
| OPL | | | | | | | | | | |
| Foveal | 29.8±6.5 | >0.05 | 30.1±6.2 | >0.05 | 28.1±7.4 | >0.05 | 29.2±7.7 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 32.7±7.3 | >0.05 | 35.4±7.5 | 0.03 | 31.3±5.9 | >0.05 | 35.6±6.2 | 0.02 | >0.05 | >0.05 |
| INL | | | | | | | | | | |
| Foveal | 26.9±5.2 | >0.05 | 27.2±5.6 | >0.05 | 27.5±6.3 | >0.05 | 28.6±6.7 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 40.1±4.9 | >0.05 | 44.3±5.1 | 0.01 | 44.5±3.5 | 0.02 | 47.8±4.1 | 0.001 | 0.03 | 0.01 |
| IPL | | | | | | | | | | |
| Foveal | 21.7±4.6 | >0.05 | 21.9±4.7 | >0.05 | 20.9±5.5 | >0.05 | 21.1±5.8 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 39.3±5.7 | >0.05 | 40.2±5.4 | >0.05 | 39.5±5.7 | >0.05 | 41.3±6.1 | 0.02 | >0.05 | >0.05 |
| GCL | | | | | | | | | | |
| Foveal | 18.5±4.7 | >0.05 | 18.6±4.5 | >0.05 | 17.6±4.5 | >0.05 | 18.4±5.2 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 49.3±9.7 | >0.05 | 50.2±10.1 | >0.05 | 50.0±9.3 | >0.05 | 50.6±8.9 | >0.05 | >0.05 | >0.05 |
| RNFL | | | | | | | | | | |
| Foveal | 13.3±2.4 | >0.05 | 13.4±2.8 | >0.05 | 15.4±3.2 | >0.05 | 15.9±4.1 | >0.05 | >0.05 | >0.05 |
| Parafoveal | 21.6±5.1 | >0.05 | 22.3±5.8 | >0.05 | 21.9±5.5 | >0.05 | 22.7±6.3 | >0.05 | >0.05 | >0.05 |

TMT: Total macular thickness, RPE: Retina pigment epithelium thickness, ONL: Outer nuclear layer thickness, OPL: Outer plexiform layer thickness; INL: Inner nuclear layer thickness, IPL: Inner plexiform layer thickness, GCL: Ganglion cell layer thickness, RNFL: Retina nerve fiber layer thickness
*: Dependent t test for comparison between baseline and postoperative day 7
**: Dependent t test for comparison between baseline and postoperative day 30
&: Independent t test for comparisons between groups on day 7 and 30

is limited number of studies about effects on retina.⁵⁻⁷ Thus, this is the first study comparing effects of cataract surgery with distinct fluidic parameters on different retinal segments. Our study showed that cataract surgery using high fluidic parameters results in changes starting within inner layers and extending out layers at early postoperative period.

It is well-known that retinal thickness is increased after cataract surgery.⁹⁻¹³ However, the response of different retinal layers may differ after surgery.¹⁴⁻¹⁶ Thus, in recent years, many studies have been published about effects of

cataract surgery on different retinal segments.¹⁴⁻¹⁷ Kurt et al reported thickening at parafoveal inner nuclear layer and decreased thickness at outer plexiform layer during early postoperative period after uncomplicated cataract surgery.¹⁶ Another OCT study reported hyper-reflective spots starting at inner nuclear layer and thickened inner retinal layer at early postoperative period.¹⁵ Authors proposed that the changes occurring at inner retinal layers at early postoperative period may be due to inflammatory reaction induced by surgery. The postoperative inflammatory reactions lead increases in free radicals and prostaglandin release. In animal studies with lens extraction, it was

demonstrated acute activation of pro-inflammatory genes and proteins in inner nuclear layer, ganglion cell layer and choroid after surgery.¹⁸ Microglia, astrocytes and Müller cells are activated in inner nuclear layer after release of pro-inflammatory agents. These neuronal support cells provide connection between neurons and vascularity. In *in vitro* studies, it was demonstrated that microglial cells activated by pro-inflammatory cytokines induced a structural change in Müller cells.¹⁹ Thus, it is thought that Müller cell activation secondary to local inflammation may lead transient vasodilatation and damage at inner blood-retina barrier.¹⁵ The hypothesis was supported by increased vascular density in deep capillary plexus observed at early postoperative period on OCT angiography.^{15, 20} The inflammatory agents causing damage at inner blood-retinal barrier at early postoperative period after cataract surgery can lead vascular hyper-permeability by interrupting outer blood-retina barrier over time.²¹ Pilotto et al. reported thickening in outer retinal layer on postoperative day 30 following thickened inner retina at early postoperative period.¹⁵ In addition, many studies have shown thickening at outer nuclear and outer plexiform layers on month 1 after cataract surgery.^{15, 16, 22} In agreement with literature, it was shown that there was an increase in parafoveal DNL, DPL and INL thicknesses on postoperative day 30 in both groups and that the extent of thickening was greater in DNL and INL in high fluidic parameter group in our study (Table 4). These results showed effects of postoperative inflammation on different retinal segments after cataract surgery using high and low fluidic parameters; in addition, they also showed that the magnitude of effect was greater in high fluidic parameter group. No significant difference was found in VA at baseline and on postoperative days 7 and 30 between groups. This result may indicate postoperative thickening at inner nuclear and outer nuclear layer were clinically irrelevant.

In the literature, there is limited number of study investigated safety and effects of cataract surgery using different fluid dynamics on retina.⁵⁻⁷ In these studies, it was suggested that the increase in central macular thickness after cataract surgery was greater in high fluidic parameter group when compared to low fluidic parameter group; however, the difference did not reach statistical significance. In our study, there was no significant difference in foveal and parafoveal total macular thickness on postoperative day 7 and 30 between groups. However, in segmentation analysis, a significant increase was observed in parafoveal INL thickness on postoperative day 7 in high fluidic parameter group (Table 4). We think that increased INL thickness in high fluidic parameter group may be due to either secondary to inflammation induced during surgery

or effect of increased IOP related to high bottle level (110 cmH₂O ~ 75 mmHg, 60 cmH₂O ~ 45 mmHg) on retinal micro-circulation.

Although exact mechanisms underlying changes in inner retinal layer during acute phase are unknown, some researchers demonstrated that the changes in inner retinal layer resulted from intracellular edema of cells at inner nuclear layer in animal studies.²³⁻²⁵ Thus, we think that the increased INT thickness may be associated with intracellular swelling processes caused by retinal ischemia-reperfusion injury due to IOP elevation resulting from high bottle level during surgery. The fact that INT thickening was observed at parafoveal region but not in avascular foveal zone suggests that the increased thickness may be related to vascular circulation.

On the other hand, the increased parafoveal INT thickness at early postoperative period in high fluidic parameter group may be associated to transient IOP elevation. Pandita et al. reported that IOP fluctuations and absolute IOP levels after cataract surgery with low fluidic parameters were lower when compared to high fluidic parameters.²⁶ In addition, they found less anterior chamber reaction and anterior segment findings after cataract surgery with low fluidic parameters.²⁷ Based on these results, cataract surgery with high fluidic parameters and bottle levels may lead increased INT thickness due to increased inflammation and transient IOP elevation through above-mentioned mechanisms at early postoperative period. In our study, the likelihood of transient IOP elevation in high fluidic parameter group cannot be excluded although there was no significant difference in IOP on postoperative day 7 between groups. Thus, our study showed that there was an identifiable and measurable effect of high aspiration flow rate and bottle level on retina at early period after cataract surgery.

This study has some limitations including small sample size, lack of controls and limited follow-up. Although no clinically relevant effect of changes in thicknesses of different retinal segments at early postoperative period on visual acuity was observed in our study, the lack of analysis of the effect on contrast sensitivity is an important limitation. Another limitation is the exclusion of patients with dense cataract in order to perform preoperative retinal segmentation. Again, other limitations include lack of quantitative assessment of inflammation following surgery in high and low fluidic parameter groups and lack of OCT angiography and assessment of vascular density alterations.

In conclusion, our study showed increased retinal thickness starting at parafoveal inner nuclear layer at

early postoperative period and extending to outer nuclear layer, as being more prominent in high fluidic parameter group. Although this study showed role of postoperative inflammation in the pathophysiology of inner retinal layer thickening after surgery, acute IOP elevations during and after surgery caused by high bottle level may also be involved. Although these changes are clinically irrelevant regarding visual acuity, further studies with longer follow-up are needed to evaluate long-term effects.

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