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Foveal Changes after Uneventful Phacoemulsification Surgery for Senile Nuclear Cataract

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ABSTRACT

Objective: To describe foveal thickness and foveal anatomical changes after uneventful phacoemulsification surgery.

Design: Interventional case control study.

Participants: Both eyes of healthy phakic patients presenting to the American University of Beirut Medical Center Eye clinic for phaco-emulsification surgery in one eye (the study eye). The fellow eye served as control.

Methods: OCT images of the macula were taken pre-operatively, then on a weekly basis for 12 weeks post-operatively.

Outcomes: post op foveal thickness and morphological changes.

Results: From the originally recruited 66 patients, 52 patients (104 eyes) completed the study. A transient increase in foveal thickness was observed in 36/52 (69%) eyes mostly between weeks 4 and 7 post operatively. Twenty-seven eyes developed anatomic changes including: microcysts in 15 eyes (55%), regular cysts in 6 eyes (22%), and epiretinal membranes in 6 eyes (11.5%). Changes appeared as early as 1 week post operatively, and lasted on the average 4 weeks.

Conclusion: Uncomplicated cataract surgery can lead to transient thickening of the macula as well as morphological changes.

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Introduction

Phacoemulsification surgery is the most common intraocular surgery performed today, with reported good visual outcomes [1,2]. However, even when uneventful, this intra-ocular surgery is thought to be associated with an inflammatory process, manifested in part by the presence of fluid in the fovea, and/or the development of morphologic abnormalities in the same anatomical area [3,4]. In fact, Chu et al. demonstrated that the aqueous fluid from patients who underwent cataract surgery had increases in pro-inflammatory cytokines, some of which were predictive of the development of post-operative macular edema [5]. Other potential causes of post-operative macular edema discussed in the literature are

the following: tractional forces on the macula during surgery, disruption of the blood retinal barrier, hypotony, and iris trauma [6,7]. This inflammation translates clinically as an increase in foveal thickness or a change in the foveal architecture. While frequently detected by a thorough examination, these findings can be subclinical and transient, seen only when using detailed and frequent imaging of the retina [8].

Spectral Domain Optical Coherence Tomography (SD-OCT) lends itself as a non-invasive, high resolution imaging modality with a fast and dense volumetric scanning capability of the macular area, characterized by easy image acquisition and interpretation, as well

as high reproducibility [9-12]. It has largely replaced the traditional use of fluorescein angiography for the diagnosis of asymptomatic and symptomatic edema [12,13]. Researchers have estimated the prevalence of subclinical/asymptomatic post operative macular edema to range between 3.1-41% [14-17]. Clinical and symptomatic Irvine-Gass however, was shown to affect a smaller 0.1-2% patient subset [17]. CME is reported in the literature to peak between 4 and 6 weeks post-operatively [2,13,18]. Vukicevic et al. found that on average central foveal thickness increased by around 7% before going back to baseline within 6 months of surgery [16]. Absolute phacoemulsification power or time is considered a risk factor for the development of post-operative macular edema and was directly correlated with post-operative thickening of the macula [19]. However, many studies comparing femtosecond versus conventional phacoemulsification showed no difference in the rate of POME in both groups despite the use of less phacoemulsification power in the former – likely due to the laser power as a counterpart [20]. Our aim in this study was to look at the detailed thickness and anatomical changes that could develop in the macula after uncomplicated phacoemulsification surgery using serial SD-OCT imaging. We also looked at the ultrasonic power and phacoemulsification time used in surgery and their relationship to postoperative macular edema and other morphologic changes.

Methods

Patients Recruitment

This prospective study was in agreement with the declaration of Helsinki. After IRB approval from the American University of Beirut, elderly patients with bilateral senile nuclear sclerosis cataract, who presented for phacoemulsification surgery at the American University of Beirut Medical Center between January 2018 and January 2020 were invited to participate in the study. The severity of the cataract was graded according to the LOCS III classification system [21]. Eyes with isolated NO3 and NC3 in the eye to be operated were recruited into the study. Both eyes of study subjects underwent serial SDOCT imaging: The eye that was going to be operated (the study eye) would be followed up for any foveal thickness change or anatomical abnormality development after surgery, and the contralateral eye would be imaged on a weekly basis and served as control. Patients also underwent a comprehensive ophthalmologic evaluation pre-operatively, and then at 1, 4 and 12 weeks post operatively. Inclusion criteria were patients aged above 65 years and willingness to have repeated serial weekly SDOCT for 3 months to both eyes, as well as to come back for periodic ophthalmologic evaluations following the previously mentioned set plan. Exclusion criteria were patients with any macular pathology in either eye, patients with diabetes mellitus, patients that had less than 21 mm or more than 26 mm axial length as measured during IOL calculation, and patients with non-lenticular media opacities hindering proper imaging of the macula in either eye. Patients with any suspected complication during phacoemulsification surgery were also removed from the study.

Imaging

SD-OCT was repeated weekly for 12 weeks to both eyes.

Acquisition

SDOCT was done using the Cirrus 5000 machine (Zeiss, Germany). In short, after dilation of the pupils by placing the patient in a dark room, study subjects underwent an SD-OCT macular cube study. A 6mm x 6mm cube of the central macular area consisting of 128 B-scans with each B-scan consisting of 512 A-scans, was taken for each eye by one skilled technician with training in SD-OCT imaging. After subjects maintained steady fixation on an internal fixation target, scans were acquired by centering them on the umbo and then improving the quality of the image by optimizing the focusing and correcting for the patients' refractive error. Images were stored and sent electronically to the reading station to be interpreted at a later date.

Image Interpretation and Analysis

After removing patient identifiers, precisely patients' names, medical record number and gender, images for each patient were sent to a reading station. Readers were retina specialists not involved in the study. They were blind to whether the image belonged to an eye that underwent surgery or not. Interpretation of the SD-OCT was done using the standard viewing software. Readers were allowed to adjust electronically image quality and views.

Measurement of the foveal thickness was obtained from subfield 1 (the central subfield) of the SD-OCT ETDRS grid (Figure 1). These were tabulated into an excel sheet for statistical analysis looking at the thickness change with respect to this specific foveal region over time. Ten percent change in foveal thickness from the original value was considered significant at any point in time. Anatomical abnormalities were assessed in every line scan of the macular cube. Any morphological change, be it at the intra-retinal or epiretinal level was considered significant. Cystic changes were defined as discrete lacunar areas of hypo reflectivity with clear boundaries present at least on 2 adjacent scans. These were measured using their largest diameter. Cysts were subdivided into microcysts and "regular" cysts based on their size. Cysts that measured between 30 to 90 μ m in GLD were labeled as microcysts. Those measuring more were labeled as a "regular" cyst. Eyes with both microcysts and larger cysts were labelled as having "regular" cysts. Epiretinal membrane was defined as a hyper-reflective layer on the surface of the retina. Even if associated with cysts (be it of regular size or micro cysts), the diagnosis of ERM superseded the latter. Figures 2a, 2b and 2c illustrate each of these findings respectively. All anatomical changes were tabulated for qualitative analysis.

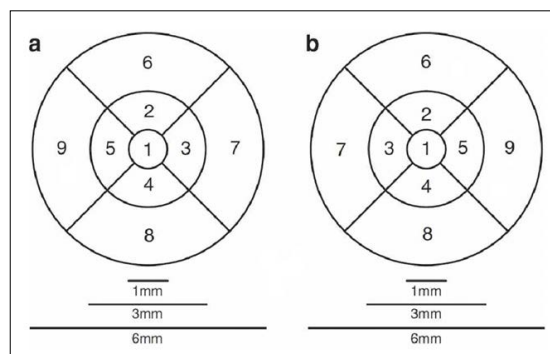


Figure 1: ETDRS Grid showing OCT Subfields in the Right Eye (a) and Left Eye (b)

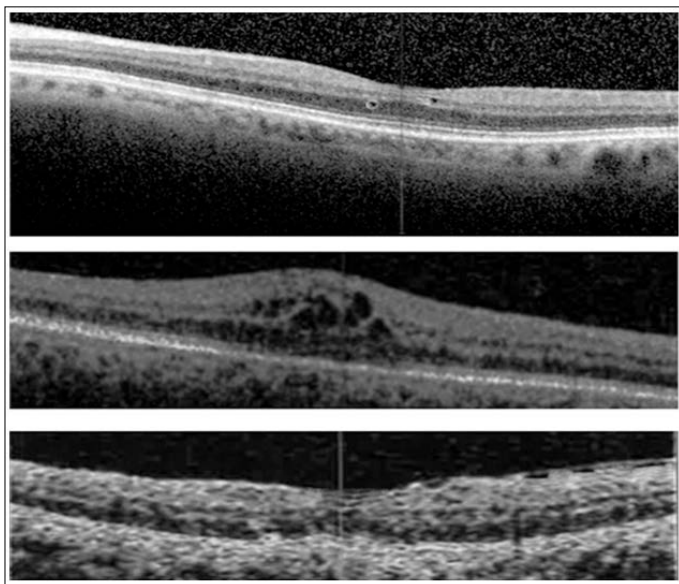


Figure 2a, 2b, 2c: Showing Respectively, Examples of Microcysts, Cysts and Epiretinal Membrane

Phacoemulsification Surgery and Post-Operative Care

All surgeries and the post operative care were performed by a single surgeon. Before surgery, tropicamide 1%, phenylephrine 10% and indomethacin eye drops would all be instilled in the eye undergoing surgery. All procedures were performed under retro-bulbar anesthesia (2% Xylocaine and 0.5% Bupivacaine injection) and Propicaine eye drops. The surgeon used the “divide and conquer” technique. The same visco-elastic agent was used (Amvisc Plus®) on all patients. All patients had a one-piece acrylic intraocular lens (Acrysof, Alcon) implanted in the bag. In addition, at the end of surgery, all patients had an intra-cameral injection of 0.1 cc of Moxifloxacin as means of prophylaxis against endophthalmitis. Specific data from the surgery namely phacoemulsification time and average ultrasonic power used was collected and tabulated for each patient. Post op eye drops regimen was standardized for all patients: Moxifloxacin eye drops 4 times daily for a one-week period and 1% Prednisolone acetate eye drops 6 times daily for 1 week with a gradual taper by one drop per day on a weekly basis for a period of 6 weeks. As mentioned previously, post operative examinations were done at the 1 week, 4 week and 12 weeks’ time intervals after surgery. During these post op comprehensive evaluations, if a patient was found to have cystoid macular edema, with some evidence of decreased vision with either cysts or macular thickening detected by examination, or by an OCT study done then at the discretion of the clinician, the patient would receive indomethacin and Prednisolone acetate 1% eye drops 3 times daily for a period of 12 weeks.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS), version 28. Categorical variables were reported as number and percent, whereas continuous variables were reported as mean and Standard Deviation (SD). Difference in thickness at two different times was assessed using a paired t-test. Moreover, difference between two groups was assessed using the independent t-test. P-value <0.05 was considered statistically significant.

Results

From the originally recruited 66 patients, 52 patients (104 eyes) completed the study: 9 patients were lost to follow up (including patients who could not keep up with the regular weekly OCT

visit for 12 weeks), 2 patients had their pre-operative images poised by a relatively dense cataract preop, 2 patients were found to have diabetes during the course of the study, and one patient had a suspicion of a rent in the posterior capsule. Patients’ age ranged from 65 to 84 years (mean of 73 years; SD 6.16 years). There was a 1.8:1 male to female ratio. There was no difference in the surgical parameters used. Table 1 summarizes the patients’ demographic characteristics.

Table 1: Demographic Characteristics

Variables		N (%)
Age	Mean ± SD	73.02 ± 6.16
	Range	61-84
Gender	Female	20 (38.5%)
	Male	32 (61.5%)
Eye	OD	23 (44.2%)
	OS	29 (55.8%)

Thickness Changes

Figures 3a and 3b summarize the findings. The average preop thickness was 259.8 μm (SD 25.9) for all 52 patients at study entry, increasing to a post op value of 280.9 μm (SD 50.625) on study closure, suggesting a significant overall increase by 8% in average thickness (p=0.009). There was at least a 10% increase in foveal thickness in 36 of the 52 (69%) operated eyes. Of these, only 10 received medical treatment (27.8%). This increase normalized with time, lasting on average a span of 4 weeks range 1 to 11 weeks, SD 3.03 in 24 (66%) patients. Subjects who received treatment did not have a different course than the ones who did not. Three patients (5.77%) had a 10% decrease in their foveal thickness. Thirteen patients (25%) had no change in their foveal thickness throughout the study. The increase in foveal thickness was noted as early as 1 week postoperative on OCT in 4 of the eyes, and as late as 8 weeks post op in 1 eye. Thickness was noted to gradually increase to reach a peak between weeks 4 and 7 in 33 eyes. The thickness went back close to baseline within 12 weeks except in 5 eyes where it lingered beyond study closure at 12 weeks. In contralateral eyes foveal thickness remained stable throughout the study period (figure 3b).

Morphologic Changes

Morphologic changes were detected in 27 eyes. Anatomical findings comprised microcystic changes in 15 eyes, regular cysts in 6 eyes and epiretinal membranes in 6 eyes. Microcystic changes appeared as early as one week post op culminated at 7 weeks then disappeared with time (lasting an average of 3 weeks) except if they were associated with a mechanical factor from an ERM. Regular cystic changes appeared as early as 1 week post op, lasted 4 weeks and were not present at study closure. Epiretinal membranes appeared as early as 1 week post op. All eyes that had an anatomical abnormality had an increase in thickness with the exception of eye that exhibited microcystic changes without any significant change in thickness throughout the study. On the other hand, the contralateral eyes had no morphological changes seen throughout the study.

Phacoemulsification Parameters

Table 2 shows the phacoemulsification data and ocular anatomical data of all the patients. There was no statistically significant difference in phacoemulsification power used or phacoemulsification time in eyes with a thickness increase as compared to the rest of the study eyes (p=0.91 and p=0.49

respectively). Similarly, there was no statistically significant difference in phacoemulsification power ($p=0.69$) and phacoemulsification time ($p=0.62$) between eyes that developed morphological changes compared to those that did not.

Table 2: Ocular Characteristics & Phacoemulsification Surgical Parameters. Eyes with Increased Foveal Thickness are Highlighted in Yellow, While Eyes that Developed Morphological Abnormalities are Written in Red

	Ultrasound Time	Average Power	A/C Depth	AL
1	98	22	2.9	23
2	79	18	3.2	24
3	125	30	2.4	22.1
4	121	25	2.6	22.3
5	86	20	2.8	23.3
6	92	18	2.4	24
7	82	24	3.2	24.5
8	130	22	3.4	25.1
9	101	26	2.8	21.9
10	88	34	3.3	22.6
11	79	18	2.5	23.2
12	80	20	3.1	23.5
13	170	24	2.8	22.8
14	137	25	3.3	24.1
15	63	17	2.5	23.1
16	97	19	3.3	24.8
17	135	23	2.9	23.1
18	89	18	3.1	24.7
19	115	26	2.7	22.2
20	49	16	2.7	23.2
21	88	20	2.5	24.1
22	99	25	2.3	21.8
23	108	25	3	23
24	77	26	2.8	22.7
25	119	24	2.7	22.8
26	89	20	2.7	23.3
27	150	25	3.1	23.7
28	168	26	2.8	22.8
29	77	18	3.2	24.3
30	76	16	2.8	23.1
31	90	24	3.3	23.8
32	129	25	2.8	24.1
33	200	24	2.7	22.9
34	88	26	3	24.3
35	43	18	2.4	22.1
36	64	16	4.36	24.5
37	87	20	2.3	23.4
38	156	25	2.7	22.9
39	201	24	3.2	24.7
40	94	25	2.9	23.3
41	88	25	3.1	24.3

42	80	18	3.2	24.1
43	73	16	3.4	23.8
44	97	20	2.6	22.9
45	69	28	2.9	22.6
46	119	18	3.2	24.6
47	190	26	2.2	22.1
48	78	24	2.6	23.2
49	145	26	3.3	23.8
50	88	24	3.2	23.7
51	123	22	3.1	23.5
52	72	18	3.3	24.2

Treated Patients

Ten patients underwent treatment and they all had an increase in thickness of more than 10%. (range 15-136%). With the exception of one case, nine had morphological changes. Three had regular cysts, 3 had microcysts and 3 had an epiretinal membrane.

Discussion

This prospective study included 52 healthy subjects that underwent standardized uneventful phacoemulsification in 1 eye and were followed with weekly SD-OCT looking at changes in foveal thickness and morphology developing within 12 weeks of surgery. The contralateral non-operated eyes served as controls. We noted a transient increase in foveal thickness in 69% of operated eyes that was detected between week 4 and week 7 postoperatively and resolved by the 12-week visit in the majority of cases (86.11%). Interestingly, we even noted thickening as early as in the first week post-operatively on the OCT in 4 patients, or 11.11% of our sample, which was not reported before in the literature. Our findings confirm previous reports using time domain OCT, namely a transient increase in foveal thickness that gradually normalizes [14-16,19]. In contralateral eyes foveal thickness remained stable throughout the study period (figure 3a and 3b). Even when the change was modest, less than 10%, in the operated eye, a similar increase was not manifested in the unoperated eye further confirming the role of surgical trauma. This transient change noted following uneventful phacoemulsification has been attributed to several factors. First, because of its invasive nature, this procedure bears an expected tissue inflammatory response from the surgical insult, demonstrated by the release of prostaglandins even after a smooth operation [3-5,22]. Second, the implanted intraocular lens, being a foreign body material, can induce a possible toxicity leading to the release of inflammatory mediators [23]. Finally, the disturbance of the vitreous architecture could contribute to postoperative macular changes, as could photic retinal damage from the surgical microscope light [23,24].

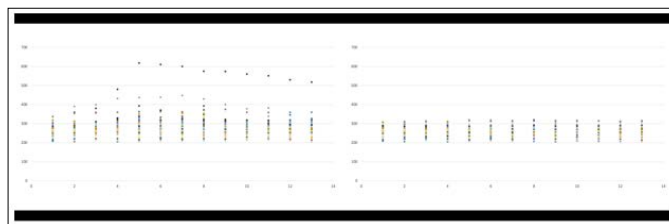


Figure 3a 3b: Eyes with increased Thickness (3a) and their Fellow Eyes (3b)

In our series, there was no relationship between phacoemulsification time and foveal thickness or morphological changes. Similarly, there was no relationship with ultrasonic energy used during surgery. The authors believe that the number of eyes in the study might have been too small to detect a correlation between the ultrasonic insult and macular changes -be it time or power. Both former parameters did not show any impact on post-operative foveal thickness but the narrow spectrum of lenticular opacities chosen as the enrolment criteria made variations in phacoemulsification parameters small. Nonetheless, similar to our findings, Gharbiya et al. also did not find a correlation between effective phacoemulsification time and phacoemulsification power and changes at the macula in their sample of 40 healthy patients [25].

Our most common anatomical finding was microcysts that were seen in 55% of the eyes that had anatomical abnormalities detected. These changes were associated with the least increase in foveal thickness. In addition, the increase in thickness associated with microcysts was transient, lasting at most 4 weeks. Other authors have linked such an abnormality with an inflammatory status of the retina such as the one seen in multiple sclerosis and neuromyietis ophthalmica [26]. Regular sized cysts were less frequently noted in our sample (only in 22%) and were associated with a more pronounced increase in foveal thickness. Furthermore, epiretinal membranes developed as early as week 1 post-operatively in our sample and caused the biggest increment in thickness. The authors acknowledge that in some cases, an ERM may have been present preoperatively as an undetectable cellophane change that evolved into thicker detectable ERM after surgery, which has been reported previously [27]. Alternatively, vitreomacular interface abnormalities may have been triggered by the surgery leading to more visible ERM.

The authors acknowledge several limitations in this study. First, the number of patients recruited was relatively small, and therefore could have limited strong correlation powers. This is possibly related to the challenge of finding previously healthy elderly patients able to commit to weekly visits for a span of 3 months. Second, the authors purposely chose patients with a narrow age range and comparable lenticular opacities in order to subject all patients to a somewhat similar surgical insult. This translated into a dampening of the effect of both the phacoemulsification time and average ultrasonic energy used on any of the results. Having a wider age range with a larger number of subjects could have possibly given these latter parameters more weight. Nonetheless, the healthy patients and the moderate cataract severity further supports the fact that post-operative macular inflammatory changes can be expected in smooth and uneventful surgeries. Third, while the OCT imaging modality used in this study is acceptable and widely used, newer modalities might have offered more details regarding deeper retinal layers, such as studies using the swept-source OCT. It would also be interesting to repeat this study using OCT angiography which could give insight on the changes at the level of choroidal and foveal vessels after phacoemulsification surgery. Case series (with no control eyes) have been reported using such modalities however with less frequent or shorter total follow up period [14,16,28].

In conclusion, the authors believe this work is valuable, since, to our knowledge, this is the first study that followed foveal changes postoperatively with such intense frequency for a relatively long period of 12 weeks [29,30]. Other studies have monitored thickness periodically, but generally on a monthly basis in our series, this would translate in missing at least 5 cases that experienced a

transient increase in their foveal thickness that resolved within 1 month (or less) from the time of detection. While taxing on all parties, this could at least in part explain the minor fluctuations in vision experienced by patients as they recover from surgery [31]. Further studies are needed to understand the long-term impact of such changes in foveal thickness and morphology on visual outcome following phacoemulsification.

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