Measurement of Subfoveal Choroidal Thickness After Cataract Surgery in Enhanced Depth Imaging Optical Coherence Tomography

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PURPOSE. To compare subfoveal choroidal thickness (SFCT) before and after uneventful cataract surgery using enhanced depth imaging optical coherence tomography (EDI-OCT).

METHODS. A prospective study was conducted on 115 eyes of 95 patients who had phacoemulsification. Measurements of SFCT were performed preoperatively, 1 day (D1), 7 days (D7), 1 month (M1), and 3 months (M3) after surgery using the EDI-OCT technique. Central retinal thickness (CRT) was measured before surgery and at M1 and M3.

RESULTS. The 95 patients had a mean age of 76 ± 8.3 years. The mean SFCT at baseline was 224 ± 75 μm. It showed a negative correlation with age and axial length (P = 0.03). The SFCT significantly increased after surgery with a mean value of 232 ± 76 µm at D1 (P < 0.001), 237 ± 78 µm at M1 (P < 0.001), and 232 ± 76 µm at M3 (P < 0.001). The mean CRT increased from 234 ± 48 µm at baseline to 248 ± 48 µm at M1 (P = 0.005), and 252 ± 81 µm at M3 (P = 0.001). Three (2.6%) patients developed a pseudophakic cystoid macular edema (PCME). The greatest progression of SFCT after phacoemulsification was observed for these patients. It preceded the occurrence of pseudophakic cystoid macular edema (PCME) by 1 month.

CONCLUSIONS. Mean SFCT increased after cataract surgery. The changes in baseline SFCT were greater in PCME patients and preceded the increase in CRT.

Keywords: pseudophakic cystoid macular edema, EDI-OCT, subfoveal choroidal thickness, central retinal thickness

Pseudophakic cystoid macular edema (PCME) is the most common cause of decreased vision following cataract surgery.1 The incidence of clinical PCME, associated with visual loss up to 20/40 or worse, ranges from 0.1% to 2.3%.2,3 Its peak occurs approximately 4 to 6 weeks after surgery.1 Angiographic incidence of PCME is much higher reaching 15% to 30%4,5 with a peak 10 weeks after surgery.3 Today, the most reliable tool to detect PCME, defined as an increased thickness and volume of the fovea often associated with cysts, is optical coherence tomography (OCT). Tomographic incidence of PCME ranges from 4% to 11%,6,7 but can reach 41% of patients 6 weeks after surgery.8 Increase in central retinal thickness (CRT) is detectable at postoperative early periods, after the first day9 or the first week after uncomplicated phacoemulsification.7

The exact pathogenesis of PCME remains unknown and is likely to be multifactorial.1 Indeed, many factors have been proposed such as vascular instability, vitreomacular traction, ocular hypotony, and UV light damage.10 However, postoperative inflammation appears to play a major role in its development.10,11 The surgical procedure releases inflammatory mediators, such as prostaglandins, leukotrienes, and cytokines, which leads to the breakdown of the blood–aqueous barrier and of the blood-retinal barrier.11,12 Recently, an acute expression of pro-inflammatory genes and proteins has been found in the neurosensory retina as well as in the choroid of mice undergoing lens extraction.13 This last study suggests that the choroid may also be involved in the inflammatory response after cataract surgery. However, its contribution to the development of PCME is hypothetical and needs to be investigated.

Enhanced depth imaging OCT (EDI-OCT) was recently described by Spaide et al.14 and Margolis and Spaide.15 This new technique enables the cross-sectional structure and thickness of the choroid to be evaluated. The subfoveal choroidal thickness (SFCT) is measured vertically, at the fovea, from the outer surface of the hyperreflective line ascribed to the retinal pigment epithelium (RPE) to the hyperreflective line of the inner sclera border.14,15 Thanks to this method, the involvement of the choroid has been highlighted in several inflammatory pathologies.16,17

The purpose of the current study was to evaluate the potential changes in the SFCT after cataract surgery, using the EDI-OCT technique, and to determine if the variations of the SFCT were correlated with the development of PCME.

METHODS

We have conducted a prospective interventional study on 95 consecutive patients (115 eyes) undergoing cataract surgery in our institutional setting between January and July 2012. All the patients were informed and gave their written consent. The study was approved by the local ethics committee and adhered to the tenets of the Declaration of Helsinki.
Inclusion criterion was visually significant cataract. Patients with very dense cataract precluding visualization of retinal fundus were excluded. Patients with diabetes mellitus were not excluded.

A complete ophthalmologic examination was performed before surgery including visual acuity, IOP measurement, slit-lamp evaluation and fundus examination. Subject characteristics including age, sex, and existence of associated ocular diseases were recorded. All participants were asked about their medical history and their current medication.

The surgical procedure consisted of phacoemulsification with clear cornea 2.2-mm self-sealing incision and intracapsular lens implantation. The surgeries were performed under topical anesthesia. At the completion of surgery, 0.1 mL/1 mg of cefuroxime (Cefuroxime Mylan; Mylan, Saint-Priest, France) was injected in the anterior chamber. Postoperative treatment consisted of dexamethasone and neomycin eye drops (Chibrodron; Thea, Clermont-Ferrand, France), tropicamide eye drops (Mydriaticum, Thea) and indomethacin eye drops (Indocollyre 0.1%; Chauvin, Montpellier, France) three times a day for 1 month.

The OCT images were obtained using the Spectralis HRA-OCT (Heidelberg Engineering, Heidelberg, Germany). Choroidal imaging was performed using the EDI mode of the HRA-OCT that automatically re-inverts the inverted images and enables EDI-OCT images to be captured directly. Thirteen sections and 768 A-scans, each composed of the 100 averaged scans obtained using eye tracking, were obtained in a 5° × 30° rectangle encompassing the macula and optic nerve. The intersection point of the horizontal and vertical scan was checked manually before image acquisition. Subfoveal choroidal thickness was measured from the outer surface of the hyper-reflective line ascribed to the RPE to the hyperreflective line of the inner sclera border. The section going directly through the center of the fovea was selected for this measure. Subfoveal choroidal thickness was measured before surgery (D-1), 1 day (D1), 7 days (D7), 1 month (M1), and 3 months (M3) after phacoemulsification. Choroidal measurements were performed on both eyes, the fellow eyes constituting a control group. Central retinal thickness was also measured before surgery (D-1), and 1 and 3 months after phacoemulsification (M1 and M3). Twenty-five sections and 512 A-scans were obtained in a 20° × 20° square centered onto the fovea. The measurements were done in triplicate by two independent examiners.

As described by Kim et al., the diagnosis of PCME was set in case of clinical observation of macular cystoid changes together with decreased visual acuity, associated with an increase greater than or equal to 40% in baseline CRT. All data were expressed as mean ± SD. A d’Agostino-Pearson test was used to assess the normal distribution of variables. Depending on the distribution of continuous data, intergroup mean comparisons were done using Student’s t-test or Mann-Whitney U test, if required (SPSS software version 17.0; SPSS, Inc., Chicago, IL, USA). Comparisons of choroidal thickness at baseline to several criteria such as age and axial length were done by simple linear regression test (univariate analysis). For overtime comparisons of data (SFCT, CRT) of the same patient, a paired Student’s t-test was used at each time point versus preoperative values (D-1). All eyes were treated independently in particular for patients with both eyes included in the study. A P value less than 0.05 was considered to be statistically significant.

**RESULTS**

The study included 115 eyes of 95 patients. There were 39 males and 56 females, who had a mean age of 76 ± 8.3 years. The mean axial length was 23.5 ± 1.2 mm. Thirty-two eyes from 26 diabetic patients were operated. Among these 32 diabetic eyes, seven eyes presented with a mild to moderate diabetic retinopathy, three eyes were treated with panretinal
photocoagulation for at least 6 months before cataract surgery, while 22 eyes did not show any signs of diabetic retinopathy.

Twenty patients had bilateral cataract surgery, with a delay superior to 15 days between the two procedures. There were no preoperative complications in any of the study patients.

Before surgery, the mean SFCT was 223.6 ± 74 μm for the study eye and 225.3 ± 82 μm for the fellow eye (P = 0.43). The

**Figure 2.** Scatterplot showing mean subfoveal choroidal thickness versus axial length preoperatively.

**Figure 3.** Box plot showing the distribution of SFCT measurements in all operated eyes. Data express differences in the set of individual values at D1, D7, M1, and M3 after surgery versus preoperative values (D-1). Each box delineates the 25th and 75th percentiles. The horizontal line represents the median value. Error bars show the fifth and 95th percentiles. The stars indicate that there is a significant difference between the mean preoperative SFCT (D-1) and the mean SFCT measured at D7, M1, and M3 after surgery.
mean SFCT was 208.9 ± 73 μm in 32 diabetic eyes and 229.6 ± 75 μm in 83 nondiabetic eyes (P = 0.18). The preoperative SFCT was inversely correlated with age (P = 0.03) and with axial length (P = 0.0287; Figs. 1, 2).

After surgery, the mean SFCT for all eyes remained stable to 223.1 ± 75 μm at D1, then significantly increased to 232.1 ± 76 μm at D7, 236.8 ± 78 μm at M1, and 235.2 ± 76 μm at M3 (P < 0.05 for D7, M1, and M3 when compared with preoperative values; Fig. 3). The greatest progression of SFCT was observed between D1 and D7 after surgery. For the nonoperated fellow eye, there was no significant variation in mean SFCT at any time (data not shown).

For the 32 diabetic eyes, a similar trend in SFCT changes was observed (Table 1). After surgery, the mean SFCT remained stable to 211.4 ± 74 μm at D1, then significantly increased to 219.2 ± 79 μm at D7, 228.6 ± 77 μm at M1, and 224.1 ± 77 μm at M3 (P < 0.05 for D7, M1, and M3 when compared with preoperative values; Fig. 4). The greatest progression in SFCT was observed between D7 and M1 after surgery.

The SFCT changes for the 83 nondiabetic eyes were also significantly higher at D7 (237.0 ± 75 μm), M1 (239.7 ± 77 μm), and M3 (236.6 ± 76 μm) after surgery compared with before surgery (229.6 ± 75 μm; P < 0.05; Table 1 and Fig. 5).

Increase in baseline SFCT was greater in the diabetic group (10.3 ± 14 μm between D-1 and D7; 14.2 ± 15 μm between D-1 and M1, and 14.2 ± 15 μm between D-1 and M3) than in the nondiabetic group (5.8 ± 13 μm between D-1 and D7; 11.1 ± 20 μm between D-1 and M1; 11.1 ± 22 μm between D-1 and M3; Table 2). However, the difference in mean SFCT between diabetic and nondiabetic eyes was not significant during the postoperative period (P = 0.38 at D1, P = 0.17 at D7, P = 0.46 at M1, and P = 0.51 at M3).

For the 20 patients undergoing bilateral cataract surgery, the same trend of SFCT changes was observed in each eye after surgery. The choroidal thickness of the nonoperated eye did not vary after the first eye was operated, just as the choroidal thickness of the first operated eye did not vary after the second eye was operated.

Linear regression of explanatory variables affecting SFCT changes after cataract surgery found only age as a significant independent predictor (P = 0.049). Subjects younger than 70 years were more likely to have an increase in SFCT than

### Table 1. Mean Subfoveal Choroidal Thickness (±SD) in Micrometers at Baseline and After Cataract Surgery for All Eyes, Nondiabetic Eyes, and Diabetic Eyes

<table>
<thead>
<tr>
<th></th>
<th>All Eyes, n = 115</th>
<th>Nondiabetic Eyes, n = 83</th>
<th>Diabetic Eyes, n = 32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>223.6 ± 75</td>
<td>229.6 ± 75</td>
<td>208.9 ± 73</td>
</tr>
<tr>
<td>D1</td>
<td>223.1 ± 75</td>
<td>227.8 ± 74</td>
<td>211.4 ± 74</td>
</tr>
<tr>
<td>D7</td>
<td>232.1 ± 76</td>
<td>237.0 ± 75</td>
<td>219.2 ± 79</td>
</tr>
<tr>
<td>M1</td>
<td>236.8 ± 78</td>
<td>239.7 ± 78</td>
<td>228.6 ± 77</td>
</tr>
<tr>
<td>M3</td>
<td>235.2 ± 76</td>
<td>236.6 ± 76</td>
<td>224.1 ± 77</td>
</tr>
</tbody>
</table>

**Figure 4.** Box plot showing the distribution of SFCT measurements in 32 diabetic operated eyes. Data express differences in the set of individual values at D1, D7, M1, and M3 after surgery versus preoperative values (D-1). Each box delineates the 25th and 75th percentiles. The horizontal line represents the median value. Error bars show the fifth and 95th percentiles. The stars indicate that there is a significant difference between the mean preoperative SFCT (D-1) and the mean SFCT measured at D7, M1, and M3 after surgery.
patients older than 70 years. Diabetes and axial length did not reach statistical significance.

Before surgery, the mean CRT was 233.8 ± 48 μm for all eyes. It significantly increased at M1 and M3 after phacoemulsification to 247.8 ± 78 μm (P = 0.0048) and 251.6 ± 81 μm (P = 0.0146), respectively (Table 3; Fig. 6). The mean CRT for diabetic (n = 32) and nondiabetic eyes (n = 83) was 234.5 ± 41 μm and 233.5 ± 51 μm before surgery, 243 ± 45 μm and 250 ± 88 μm 1 month after surgery, and 247.5 ± 48 μm and 253 ± 91 μm 3 months after surgery. For diabetic and nondiabetic eyes, the increase in baseline CRT was statistically significant at M1 but not at M3, due to larger SDs and smaller number of eyes in each groups (Fig. 6).

Three patients (2.6%) presented with a diagnosis of pseudophakic macular edema with an increase in baseline CRT greater than or equal to 40%. All three patients encountered a decrease in visual acuity occurring 8 weeks after phacoemulsification. Two patients had risk factors for PCME: the first patient had an associated epiretinal membrane, whereas the second patient suffered from diabetes mellitus without diabetic retinopathy or maculopathy. No risk factors could be identified for the third patient. The greatest increase in SFCT was observed for these three patients at M1, respectively +118 μm (+60%), +42 μm (+24%), and +42 μm (+13%) between D1 and M1 after cataract surgery, though the CRT increased only at M2 after phacoemulsification.

Case 1: Our first patient was an 84-year-old male. His medical history was unremarkable. On OCT, an epiretinal membrane was diagnosed in both eyes without any associated distortion or thickening of the macula. His SFCT and CRT at baseline were 320 and 252 μm, respectively. Postoperative visual acuity was 20/20 at D7 and M1. It fell to 20/40 at M2. Postoperative SFCT increased to 337 μm at D7, 356 μm at M1, and 361 μm at M2. Central retinal thickness was 249 μm at D7, 250μm at M1 and increased to 500 μm at M2, with an increase in baseline CRT of 200%.

Case 2: Our second patient was a 69-year-old male. This patient suffered from diabetes mellitus. His retinal fundus did not disclose any sign of diabetic retinopathy. No macular edema was present on his preoperative OCT images. His SFCT and CRT at baseline were 250 and 229 μm, respectively. Postoperative visual acuity was 20/20 at D7 and M1. It fell to 20/32 at M2. Postoperative SFCT increased to 253 μm at D1, 257 μm at D7, 266 μm at M1 and M2. Central retinal thickness was 211 μm at D7, and increased to 216 μm at M1, and 332 μm at M2, with an increase in baseline CRT of 62%.
Case 3: Our third patient was an 80-year-old male. His medical and ocular histories were unremarkable. His SFCT and CRT at baseline were 196 and 229 μm, respectively. The cataract surgery was uneventful. Postoperative visual acuity was 20/20 at D7 and M1. It fell to 20/50 at M2. Postoperative SFCT increased to 237 μm at D7, 315 μm at M1 and M2. Central retinal thickness increased to 235 μm at D7, 245 μm at M1, and 706 μm at M2, with an increased in baseline CRT of 300% (Fig. 7).

### DISCUSSION

Very scarce data exist regarding the possible effects of cataract surgery in the choroid. In our prospective study, we found that the choroid mean SFCT, as observed in EDI-OCT, significantly increased D7 after the surgery, reached a peak at M1, and started to decrease at M3. In 115 eyes, the greatest progression of SFCT was observed between the first and the seventh day after surgery. The SFCT of the fellow unoperated eyes remained unchanged during the follow-up period, excluding any systemic factor that could have affected choroidal measurements. All our patients were treated with antiinflammatory drops (dexamethasone and indomethacin eyedrops) prescribed from the completion of surgery and over a 1-month period. These antiinflammatory treatments are known to lower postoperative antiinflammatory response. Falcao et al. did not find, in 14 eyes of 14 patients, any statistically significant changes in SFCT.19 However, it wouldn’t have been ethical to study a control group without postoperative antiinflammatory agents to account for the acute (since 30 minutes after surgery) occurrence of a posterior segment inflammation. Another explanation is that the surgical traumatism induces an inflammation of the anterior segment would lead to the inflammation of the posterior segment inflammation. Thus, phacoemulsification seems to be able to induce morphologic changes in the choroid layers. Recently, Xu et al. have disclosed interesting results on the effect of cataract surgery in the choroid. They have investigated the expression of genes that might affect the blood–retinal barriers, including cytokine IL-1β, chemokines CCL2 and SDF-1, and growth factors FGF and VEGF in the retina and the RPE/choroid of mice undergoing extracapsular lens extraction. They found that the expression of these genes was markedly upregulated in the retina and in the choroid. However, the level of upregulation was less elevated in the RPE/choroid than in the retina and was delayed in the RPE/choroid, occurring 24 hours after surgery versus 30 minutes in the retina. Xu et al. also found that the protein IL-1β, which is a pro-inflammatory cytokine, was strongly detected in the ganglion cell layer, inner cell layer, and in the choroid of operated mice eyes.

However, how cataract surgery induces retinal and choroidal inflammation is not understood. It is known that the surgical trauma induces releases of prostaglandins in the aqueous humor, that causes a disruption of the blood–aqueous barrier. This results in the accumulation of other inflammatory mediators such as endotoxin, immune complex, and cytokines in the aqueous humor. These inflammatory mediators diffuse into the vitreous cavity to reach the retina, where they are responsible for a rupture of the inner blood–retinal barrier resulting in another cascade of inflammatory mediators secretion together with an increased permeability from the perifoveal capillaries. The outer blood–retinal barrier has also been shown to be disrupted as a consequence of postcataract surgery inflammation. Thus, the inflammation response of the anterior segment would lead to the occurrence of a posterior segment inflammation. Another explanation is that the surgical traumatism induces an inflammatory response with cytokine gene expression in all the structures of the eye at the same time, which would account for the acute (since 30 minutes after surgery)
inflammatory gene transcription observed in the retina after cataract surgery.\textsuperscript{13}

In our series, we have observed that the mean SFCT at baseline was correlated with age and axial length. Our data are consistent with the published literature showing that the choroid thickness decreases with decades and millimeters of axial length.\textsuperscript{23,24} We also found that, at baseline, the SCFT was thinner in diabetic patients versus nondiabetic patients. However, the difference did not reach statistical significance, probably due to the small number of diabetic patients in our study. The literature displays contradictory results on choroidal thickness in diabetic eyes. Some authors reported a choroidal thinning,\textsuperscript{25-27} while others found a thicker subfoveal choroid.\textsuperscript{28}

In our study, we encountered three cases of PCME (2.6\%) despite the use of postoperative prophylactic antiinflammatory drops. For the three patients, no surgical complications occurred, the duration of the surgery was limited to less than 15 minutes and the amount of ultrasounds delivered was low. Two of the three patients had a risk factor for developing PCME. The first one had an epiretinal membrane.\textsuperscript{2} The second patient suffered from well-controlled diabetes mellitus. Diabetic patients have a higher risk of PCME.\textsuperscript{3} It usually develops in subjects with a prior history of diabetic macular edema,\textsuperscript{29} which was not the case for our patient. For our third patient, no ocular or systemic risk factors for PCME were found. All three patients developed PCME at M2 after phacoemulsification while they encountered a decrease in their visual acuity. Surprisingly, the highest values of SCFT were observed for these patients at M1 after surgery, while no cystoid macular edema was present on the SD-OCT images. The CRT increased at M2 with a typical image of PCME on SD-OCT, while the SFCT was still elevated. It seemed that the increase of choroidal thickness preceded the occurrence of the PCME. These findings raise questions about the pathophysiological role of the choroid in the development of PCME.

One hypothesis would be a post inflammatory rupture in the outer blood–retinal membrane, which, in association with the rupture of the inner blood–retinal barrier, would enhance intraretinal accumulation of fluid. Experimental studies have suggested that the outer blood–retinal membrane plays a role in the pathogenesis of macular edema such as in diabetic patients.\textsuperscript{30} A disruption of the outer blood–retinal membrane would lead to abnormal inflow of fluid into the retina resulting in accumulation of fluid in the retinal layers.

In other pathologies, it is believed that the choroid is primarily affected by the disease and leads to secondary retinal manifestations such as subretinal edema or RPE leaks. In serous central chorioretinopathy\textsuperscript{31} or polypoidal choroidal vasculopathy,\textsuperscript{32} the choroidal thickening precedes the occurrence of retinal abnormalities. In these pathologies, the increased choroidal thickness is associated with a choroidal vascular hyperpermeability, generally arising from the choriocapillary-is.\textsuperscript{33} In our study, angiographies were not performed in PCME patients, which enabled us to see whether the increased choroidal thickness was associated with an increased choroidal hyperpermeability.

\begin{figure}
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\includegraphics[width=\textwidth]{figure7.png}
\caption{Enhanced depth imaging-OCT of the third patient presenting with PCME 8 weeks after cataract surgery. Subfoveal choroidal thickness started to increase at D7 after surgery and was maximal at M1. Central retinal thickness was unchanged at baseline, D7 and M1 after surgery. At M2, CRT increased to $706\ \mu m$ associated with cystoid cysts and subretinal fluid.}
\end{figure}
Meanwhile, we are not aware of any reports of indocyanine green angiographies, laser Doppler flowmetry, or ultrasound performed or showing increased choroidal hyperpermeability in PCME patients.

Our study has shown that the SFCT increases after cataract surgery despite prophylactic antiinflammatory eye drops, showing that cataract surgery may induces inflammatory changes within the choroid. It is the first report of an increase of SFCT in patients prior to the development of PCME. However, the relationship between the extent of choroidal thickness and the development of PCME needs to be clarified. Further studies are needed to investigate if the choroid plays a role in PCME physiopathology.

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References