Analysis of the Macula With Optical Coherence Tomography After Successful Surgery for Proliferative Vitreoretinopathy

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Objective: To use optical coherence tomography to assess the in vivo pathologic findings associated with incomplete visual recovery in patients who have undergone anatomically successful surgery to treat proliferative vitreoretinopathy.

Methods: Eligible patients were recruited in vitreoretinal outpatient clinics between April 1, 2002, and July 31, 2003. Patients were included who had undergone anatomically successful vitreoretinal surgery to treat proliferative vitreoretinopathy and, at least 3 months after surgery, had postoperative vision worse than expected (≤6/12) with no identifiable cause at clinical examination. Patients underwent optical coherence tomography, stereo fundus fluorescein angiography was performed in a cohort of patients, and angiographic findings were compared with those on the optical coherence tomograms. Relevant clinical data were collected retrospectively from patient case notes.

Results: A total of 35 patients were recruited. Optical coherence tomograms revealed cystoid macular edema in 23 patients (66%) but did not identify any other specific intraretinal disease. Location of edema (outer or inner retina), determined with stereo fundus fluorescein angiography and optical coherence tomography, correlated well.

Conclusions: Optical coherence tomography is a useful diagnostic tool for assessing poor postoperative visual acuity and can reveal disease undetected at clinical examination. Cystoid macular edema is a common finding on optical coherence tomograms in eyes with incomplete visual recovery after anatomically successful surgery to treat proliferative vitreoretinopathy.


Proliferative vitreoretinopathy (PVR) has an incidence of 5% to 10% of all rhegmatogenous detachments. It has a higher incidence after giant retinal tears and ocular trauma and has been noted as an important complication of macular translocation surgery.

Surgical success has improved significantly, with retinal reattachment rates of 81% for initial surgery and up to 90% for final reattachment. However, the visual results are less satisfactory, with visual acuity of 20/100 achieved in only 11% to 19% of eyes, whereas the Silicone Study Group found visual acuity of 10/100 or better in 25% of eyes. The reasons for poor vision after anatomically successful surgery to treat PVR remain uncertain. Within the retina, photoreceptor loss and damage, together with cystoid macular edema (CME) and other neural retinal abnormalities, such as axon retraction and sprouting, have been postulated as possible causes, as have retinal pigment epithelium (RPE) multilayering and subretinal gliosis, which often cannot be detected clinically. Epiretinal membrane (ERM) formation and retinal distortion are further potential reasons for visual loss. The effects of treatment and the use of tamponade agents such as silicone oil may also be important factors in the visual outcome of eyes undergoing multiple surgical interventions.

Optical coherence tomography (OCT) is a technique that provides high-resolution, cross-sectional images of the retinal structure and is particularly useful in examining the macula. The STRATUSOCT scanner (model 3000; Carl Zeiss Meditec, Dublin, Calif) has many advantages over the preceding model 2000 OCT scanner. It provides improved axial resolution in tissue (<10 µm compared with 10-20 µm), improved image quality (1024×786 432 pixels compared with 500×500 pixels), and shorter scanning time (0.32 seconds compared with 1.0 seconds).

We used OCT to study the maculas of eyes that had undergone successful sur-
surgery to treat retinal detachment complicated by PVR and had limited postoperative visual outcome. We proposed to identify morphologic changes in the retina and related tissues that could account for visual loss and to examine the relationship of macular anatomy to postoperative visual acuity.

METHODS

Patients were recruited from vitreoretinal outpatient clinics at Moorfields Eye Hospital, London, England, in 2 phases. Phase 1 extended from April to August 2002, and phase 2 extended from April 1, 2002, to July 31, 2003. All patients had undergone surgery to treat retinal detachment and subsequently underwent anatomically successful surgery to treat PVR. Patients were included who had poor postoperative vision (≤6/12) for which no pathologic cause was identifiable at clinical examination (slitlamp biomicroscopy and indirect ophthalmoscopy). Patients gave informed consent to the study, which was approved by the Moorfields Eye Hospital Local Research Ethics Committee.

Patient data were collected and included age, sex, preoperative best-corrected visual acuity (BCVA), lens status, PVR grade,13 and anatomical status of the retina and macula, together with the type and number of operations and use of scleral buckle, tamponade agent, and retinopathy. Duration of retinal detachment and PVR was also obtained retrospectively from case notes. In patients who underwent ret detachment of the retina, the duration of each retinal detachment was noted, as was the cumulative total duration of retinal detachment. At recruitment and OCT assessment, postoperative BCVA and anatomical status of the retina were recorded. The status of the macula was assessed with slitlamp biomicroscopy using the Volk Superfield lens (Volk Optical, Inc, Mentor, Ohio) and a 60-diopter (D) condensing lens (Volk Optical, Inc).

All patients were examined at least 3 months after their final operation. Patients recruited in phase 1 were scanned using the Humphrey 2000 OCT System scanner (Humphrey, San Leandro, Calif) with a 3-mm line along the horizontal axis through the fovea. Those recruited in phase 2 were scanned using the STRATUS/Socct model 3000 scanner, using the “radial line” scan option centered at the fovea with 6 lines, each 6-mm long. The fovea was identified as the patient’s fixation point. If the patient had poor or eccentric fixation in the scanned eye, the external fixator was used for the fellow eye. The images were aligned and normalized before analysis using the standard OCT 2000 and 3000 software. Results of OCT were analyzed and categorized independently by 2 ophthalmologists (S.E.B. and P.G.S.) with previous experience in OCT interpretation.

A grading system for the CME visible on OCT scans was developed based on histologic descriptions of CME.16 Despite the higher resolution of the OCT model 3000 scanner, individual cell layers of the retina cannot accurately be identified. We, therefore, categorized the edema on the basis of its situation in the inner or outer retinal layers (Table 1 and Figure 1).

Spearman rank correlation coefficients were examined to assess evidence between final BCVA and duration of detachment, duration of PVR, and preoperative BCVA. The Mann-Whitney test was used to assess evidence of association between final BCVA and the presence of silicone oil or the presence of CME on OCT scans and between the presence of CME and the number of retinal detachment operations. The Fisher exact test was used to assess the association between presence of CME and use of oil tamponade and time of OCT examination since surgery.

Using the Mann-Whitney test, we compared the number of retinal detachment operations in patients who achieved a final BCVA of 6/24 or better with those who achieved a final BCVA of 6/36 or worse. The Fisher exact test, 2-sided, was used to compare the dichotomized final BCVA (as described earlier) in patients in whom the OCT revealed CME with patients in whom the OCT showed no abnormality. To further investigate the OCT findings, stereo fundus fluorescein angiography (sFFA) was performed in a cohort of patients with CME at OCT, and the findings were analyzed by a retinal specialist masked to the OCT findings. We collected the same data detailed above, including a postoperative scan obtained with the OCT model 3000 scanner, in 2 control subjects, that is, patients who had undergone surgery to treat PVR and had good postoperative BCVA (≥6/9).

RESULTS

Seventeen patients were recruited between April 1, 2002, and August 31, 2002, and 18 patients were recruited between April 1, 2003, and July 31, 2003 (13 women and 22 men). At the time of scanning, 2 patients had aphakic retinal detachments, 5 had pseudophakic retinal detachments, and 28 had phakic retinal detachments. In all patients PVR grade C developed.1 The primary surgical procedure was vitrectomy in 28 eyes and scleral buckle in 7 eyes. Of the 35 patients, 33 underwent more than 1 vitreoretinal procedure. In all but 1 eye silicone oil tamponade was used, and in 19 of these the oil was removed at OCT examination. In 18 patients there was an improvement in BCVA (final BCVA compared with preoperative BCVA), 13 eyes had worse BCVA at the final visit, and 4 eyes remained unchanged. At initial examination (at the time of retinal detachment) the macula was detached in 10 eyes, and it remained so in 4 eyes during the postoperative period. Additional patient demographic data are summarized in Table 2.

Examination of the retina with slitlamp biomicroscopy at OCT in all patients revealed no obvious cause for their limited visual acuity. Results of OCT were analyzed independently by 2 ophthalmologists (S.E.B. and P.G.S.) with previous experience in OCT, and 100% concordance was found. The OCT examination revealed CME in 23 (66%) of 35 eyes; OCT was performed in these eyes 3 to 25 months after the final operation. In the 23 patients with CME, the edema was grade 1 in 3 patients, grade 2A in 1 patient, grade 2B in 1 patient, grade 3 in 15 patients, and grade 4 in 3 patients (Table 1).

Two patients with CME also had other pathologic findings visible on OCT scans. One had a lamellar macular hole and an intraretinal cyst (visible clinically), and the other patient had a lamellar macular hole. Two patients with-

### Table 1. CME Grade According to OCT Appearance

<table>
<thead>
<tr>
<th>CME Grade</th>
<th>OCT Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increased retinal thickness (without specific layer distinction)</td>
</tr>
<tr>
<td>2</td>
<td>Edema (cystic spaces) predominantly in inner or outer retina</td>
</tr>
<tr>
<td>2A</td>
<td>Inner retina</td>
</tr>
<tr>
<td>2B</td>
<td>Outer retina</td>
</tr>
<tr>
<td>3</td>
<td>Edema (cystic spaces) in both inner and outer retina</td>
</tr>
<tr>
<td>4</td>
<td>Gross cystoid spaces with disorganization of macular retina</td>
</tr>
</tbody>
</table>

Abbreviation: CME, cystoid macular edema; OCT, optical coherence tomography.
out CME had other abnormalities detected at OCT. One patient had subretinal heavy liquid, perfluoro-N-octane (also noted clinically), and the other patient had RPE clumping. The remaining 10 patients with no CME had normal OCT scans. The resolution of the OCT scans did not demonstrate other intraretinal pathologic findings that could potentially result in reduced visual acuity.

In 4 of the 23 patients with CME at OCT it was considered that epimacular traction was contributing to the edema: ERM and retinal distortion were visible at clinical examination but were not obvious on OCT scans, and further surgery (internal limiting membrane or ERM peel) was performed in an attempt to relieve the traction. This improved BCVA in 1 patient, and the CME grade changed from 3 to 1. Visual acuity in the other 3 patients remained unchanged; in 1 patient attempted ERM peel was unsuccessful (Table 3).

Preoperative BCVA was compared with final BCVA in all 35 patients, and no correlation was found (Spearman rank correlation rho = −0.017; P = .92). There was little evidence of any association among final vision and duration of retinal detachment, presence of oil, or presence of CME on OCT scans. Although not statistically signifi-

tant, there was some evidence (P = .07) of an association between final BCVA and duration of PVR (Spearman rank correlation rho = 0.306). There was a trend, however, for those patients with worst final vision (ie, ability to see hand movements or perception of light) to demonstrate CME at OCT (Figure 2).

### Table 2. Patient Demographic Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63</td>
<td>18-84</td>
</tr>
<tr>
<td>Vitreoretinal operations, No.</td>
<td>3</td>
<td>1-7</td>
</tr>
<tr>
<td>Duration detachment, mo</td>
<td>2</td>
<td>0.25-6</td>
</tr>
<tr>
<td>Duration of PVR, mo</td>
<td>2</td>
<td>0.5-36</td>
</tr>
<tr>
<td>Time from last surgery to OCT, mo</td>
<td>14</td>
<td>3-86</td>
</tr>
<tr>
<td>BCVA Preoperative</td>
<td>CF</td>
<td>PL-6/6</td>
</tr>
<tr>
<td>BCVA Postoperative</td>
<td>6/60</td>
<td>CF-6/12</td>
</tr>
</tbody>
</table>

Abbreviations: BCVA, best-corrected visual acuity; CF, counting fingers; OCT, optical coherence tomography; PL, perception of light; PVR, proliferative vitreoretinopathy.
There was a significant relationship between the number of retinal detachment operations and whether a BCVA of 6/24 or better was achieved (Mann-Whitney test, \( P = .04 \)), with those patients with poorer final vision having undergone more operations. There was little evidence of any association among the presence of CME and use of oil tamponade, number of retinal detachment operations, duration of PVR, duration of retinal detachment, or time between surgery and data analysis.

Twelve patients with CME demonstrated at OCT subsequently underwent sFFA. In 3 of these patients the angiogram was of inadequate quality to analyze accurately owing to media opacities. Overall, there was a good correlation between sFFA and OCT (Table 4, Figure 3). Six of the 9 patients had grade 3 OCT findings and had evidence of CME in both inner and outer retina.

Two control patients (patients A and B) with retinal detachment and PVR were identified; both had postoperative BCVA of 6/9. Patient A had preoperative BCVA of hand movements and a macula-off retinal detachment. This patient underwent 3 operations including use of oil tamponade and a macula-off retinal detachment. This patient underwent 2 operations without oil tamponade. The OCT scan at 6 months after the last operation was normal; sFFA was not performed.

**Table 3. Patients Undergoing Additional Surgery**

<table>
<thead>
<tr>
<th>Preoperative BCVA</th>
<th>Clinical Appearance</th>
<th>Preoperative OCT CME Grade</th>
<th>Surgery</th>
<th>Postoperative OCT CME Grade</th>
<th>Visual Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/60</td>
<td>ERM at macula</td>
<td>1</td>
<td>ILM/ERM peel very adherent to retina</td>
<td>1</td>
<td>6/60</td>
</tr>
<tr>
<td>6/60</td>
<td>Cystic retina, entire posterior pole with “fluffy” ERM</td>
<td>3</td>
<td>Attempted ERM peel and no discrete ERM identified</td>
<td>4</td>
<td>6/60</td>
</tr>
<tr>
<td>6/60</td>
<td>CME plus ERM at macula</td>
<td>4</td>
<td>ERM peel and AC IOL</td>
<td>3</td>
<td>6/60</td>
</tr>
<tr>
<td>6/60</td>
<td>ERM</td>
<td>3</td>
<td>ILM peel and AC IOL</td>
<td>1</td>
<td>6/9</td>
</tr>
</tbody>
</table>

**Table 4. Findings at Angiography Compared With Those at OCT**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Final Visual Acuity</th>
<th>OCT CME Grade</th>
<th>sFFA: Location of Edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6/36</td>
<td>3</td>
<td>Inner and outer layers</td>
</tr>
<tr>
<td>2</td>
<td>HM</td>
<td>3</td>
<td>Inner and outer layers</td>
</tr>
<tr>
<td>3</td>
<td>1/60</td>
<td>3</td>
<td>Mainly deep, some inner</td>
</tr>
<tr>
<td>4</td>
<td>6/36*</td>
<td>3</td>
<td>Mainly deep, some inner</td>
</tr>
<tr>
<td>5</td>
<td>6/60</td>
<td>3</td>
<td>Inner and outer layers</td>
</tr>
<tr>
<td>6</td>
<td>3/60</td>
<td>3</td>
<td>Mainly deep, some inner</td>
</tr>
<tr>
<td>7</td>
<td>6/12</td>
<td>1</td>
<td>Mainly deep, some inner</td>
</tr>
<tr>
<td>8</td>
<td>6/60</td>
<td>4</td>
<td>Mainly deep, some inner</td>
</tr>
<tr>
<td>9</td>
<td>6/12</td>
<td>1</td>
<td>Mainly deep some inner</td>
</tr>
</tbody>
</table>

**Comment**

Despite improved anatomical surgical outcomes in established PVR, visual recovery is frequently limited.\(^5\)\(^-\)\(^7\)\(^,\)\(^17\) In PVR, clinical examination can reveal the cause of poor vision in some eyes, for example, ERM formation, RPE changes, and media opacities. However, the pathologic cause of incomplete visual recovery in PVR is not usually evident clinically.

Laboratory research has identified some of the cellular events that could contribute to poor visual outcomes in retinal detachment with PVR. These processes are not usually identifiable clinically. Subretinal disease such as RPE multilayering can occur, inhibiting photoreceptor recovery and retinal reattachment.\(^8\) Photoreceptors can reach malpositioned relative to the underlying RPE, potentially producing a Stiles-Crawford effect whereby light hitting photoreceptors obliquely is inefficient at stimulation compared with light reaching photoreceptors axially.

Experimentally, photoreceptor apoptosis has been demonstrated in retinal detachment and may have an important role clinically in retinal detachment and PVR.\(^8\) Previous work by our group on human PVR tissue demonstrated loss of photoreceptor outer segments and destruction of inner segments, along with remodeling and extension of photoreceptor neurites toward the inner retina.\(^18\) Second-order neurons undergo “rewiring” changes that have un-
determined effects on visual function, and subretinal extensions of ERMs were also found. These remodeling changes are analogous to disease found in experimental retinal detachment. The purpose of this study was to determine whether by using OCT we could identify which of these many processes are responsible for poor visual outcome after anatomically successful surgery to treat PVR.

The Zeiss OCT model 3000 scanner has a theoretical longitudinal resolution of less than 10 µm in tissue; however, in clinical use this was insufficient to accurately identify individual cell layers, and, therefore, OCT cannot enable identification of many of the cellular processes cited. The OCT scans did reveal pathologic findings not seen at slitlamp clinical examination.

Optical coherence tomography enables noninvasive in vivo 2-dimensional anatomical examination. However, our study demonstrates some of its limitations. The 4 patients who underwent further surgery had clinically evident ERMs, which were not well defined on OCT scans. Wilkins et al examined 186 eyes having a clinical diagnosis of ERM and found that 12 were undetectable on OCT scans and 125 were globally adherent to the retina. The globally adherent membranes were associated with macular pseudohole, a visible membrane tuft or edge, or a difference in optical reflectivity between the membrane and retina, and, thus, a diagnosis of ERM may not be apparent in these cases at routine OCT examination. In addition, OCT does not provide information regarding vascular perfusion. Two of our patients had foveal capillary nonperfusion at sFFA, and this may be an important factor in the visual outcome of PVR. Our small sample size (n = 35) and the heterogeneity of patients in terms of the characteristics of their retinal detachments and surgery may account for the failure to demonstrate associations between clinical and OCT findings (eg, the association of preoperative and postoperative BCVA and that between clinical and OCT findings). Antcliff et al compared OCT with FFA for the detection of CME in patients with uveitis and found good concordance with OCT for detecting CME (sensitivity, 96%; specificity, 100%). Overall, it seems that CME occurs in a significant proportion of patients with PVR after anatomically successful surgery and is likely an important factor in poor visual recovery.

The OCT scans did reveal pathologic findings not seen at slitlamp clinical examination. After retinal detachment surgery uncomplicated by PVR, the reported incidence of CME on sFFA varies from 16% at 6 weeks after scleral buckle to 43% at 3 to 4 weeks after buckle surgery. Campo et al reported on outcomes of vitrectomy to treat primary retinal detachment in 275 pseudophakic eyes and found a CME rate...
of 17%, detected clinically in 67% or with FFA in 33%. Other reports of CME rates after vitrectomy to treat retinal detachment in pseudophakic eyes range from 3.2% to 8%.\textsuperscript{27–29} As anticipated, the incidence of CME in retinal detachment complicated by PVR is markedly higher.

The possible mechanisms of CME in eyes with PVR may relate to the multiple surgical procedures performed and more protracted postoperative inflammation. Uveitis is associated with CME, and PVR is known to be associated with marked blood–retinal barrier breakdown. The role of retinal vascular damage or occlusion and epiperal traction is still unknown. Internal limiting membrane or ERM peel was performed in the 4 patients in whom traction was thought to be a contributing factor to CME. One patient did have substantial improvement in vision; however, BCVA in the other 3 patients remained unchanged (Table 3). From this small cohort of patients, it is impossible to draw definite conclusions, but by relieving epiperal traction further vitreoretinal surgery may hold potential for improving vision. Similarly, medical treatment to minimize or reduce CME may be useful. Hogan and Zimmerman\textsuperscript{30} in 1962, and Machemer\textsuperscript{31} in 1968, reported that cystoid degeneration may be accompanied by retinal neural tissue loss and photoreceptor atrophy, accounting for persistent poor vision. Hence, any strategy with the goal of reducing CME would be desirable.

Examinations with OCT by Wolfensberger and Gonvers\textsuperscript{24} and Hagimura et al\textsuperscript{23} found persistent localized subretinal fluid after successful retinal detachment surgery. This was not found in our study population despite more severe disease (PVR).

Optical coherence tomography is a noninvasive method of examination that can enable detection of pathologic conditions (in this study, commonly CME) not visualized at clinical examination. The additional clinical information OCT provides may help in determination of further treatment and improvement in visual outcome. The resolution of OCT model 2000 and model 3000 scanners is insufficient to elucidate the cellular processes that cause poor vision after anatomically successful surgery to treat PVR. Further research and technologic advances, in particular, the advent of ultrahigh-resolution OCT, will enable more detailed analysis of these changes.

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