Boundary Detection Errors on Optical Coherence Tomography Images in Patients With Diabetic Retinopathy

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**BACKGROUND AND OBJECTIVE:** To study the incidence of boundary detection errors produced by optical coherence tomography measurements in patients with diabetic retinopathy.

**PATIENTS AND METHODS:** One hundred sixteen eyes with diabetic retinopathy of 64 consecutive patients with diabetes mellitus were included in this retrospective study. The StratusOCT instrument (Carl Zeiss Meditec, Dublin, CA) with the macular thickness map protocol was used for the examinations. After data acquisition, each scan was analyzed using the retinal thickness (single eye) protocol to evaluate whether there was any misdetection of the retinal boundaries.

**RESULTS:** Boundary detection errors were found in 35.3% of eyes. The majority of artifacts were those caused by hard exudates (41.5%), followed by cystoid macular edema (31.7%) and proliferation (17.0%).

**CONCLUSION:** Occurrence of artifacts with optical coherence tomography measurements in cases of diabetic retinopathy is not a rare phenomenon and verification of quantitative measurements is strongly recommended.

**INTRODUCTION**

The principles of optical coherence tomography (OCT) in retinal imaging were first described by Puliafito et al. The system uses a superluminescent diode laser as a light source and cross-sectional images are produced using low-coherence interferometry. Images obtained from the scans can be subjected to post-processing and quantitative analysis. Retinal thickness analysis identifies the outer and inner boundaries of the retina, the retinal pigment epithelium, and the retinal nerve fiber layer by means of their higher optical reflectivity.

Using the commercially available StratusOCT instrument (Model 3000 with software v4.04; Carl Zeiss Meditec, Dublin, CA), retinal map analysis calculates the thickness data for six radial scans and interpolates the thickness data in the areas between the scan lines. Using this analysis protocol, retinal thickness and volume can also be calculated. The resulting thickness and volume data are reproducible and...
may be of importance for diagnostic and follow-up purposes.

In some cases, however, the software may detect the retinal boundaries incorrectly. This may be attributable to one or more of the following causes: (1) pathologic changes of the retina that produce abnormally low or high reflectivity or shadowing, leading to erroneous boundary detection; (2) decreased transparency of the optical media of the eye, in which the signal strength of the reflections from all retinal tissues is low and therefore differentiation of the layers is more difficult or impossible for the software; and (3) technical failures such as poor patient cooperation, limited operator experience, or operator error, in which artifacts may be produced by the instrument’s software and quantitative results and then become unreliable.

Diabetic retinopathy is one of the leading causes of blindness. Diagnosis is traditionally based on funduscopy and fluorescein angiography. However, OCT has recently become an increasingly popular tool in the diagnosis and follow-up of diabetic retinopathy, especially in cases of macular edema.³

The aim of our study was to detail the incidence of artifacts affecting retinal thickness measurements produced by OCT in patients with diabetic retinopathy.

**Patients and Methods**

The study was conducted in accordance with the ethical standards stated in the Declaration of Helsinki. Institutional Review Board approval was obtained for the study. Each participant was fully informed about the examination, and provided written consent.

One hundred sixteen eyes with diabetic retinopathy of 64 consecutive patients with diabetes mellitus were included in this retrospective study. The patients (36 women and 28 men) were selected from the database of the StratusOCT measurements (performed at the Ophthalmology Department at Semmelweis University in Budapest, Hungary, during 2005) without regard to the stage of their disease. Patients were examined by two operators (MS, AS) who were actively working in the medical retina field and were experienced in the use of the StratusOCT instrument and certified by the Vienna OCT Reading Center (AS as operator, MS as operator and grader). Forty-one patients were examined by one operator (MS) and 23 by the other (AS). Mean age of the patients was 59 years (range: 20 to 79 years).

The StratusOCT instrument with the macular thickness map protocol was used for the examinations. This protocol uses six radial scan lines with a scan length of 6 mm each, set 30° apart, in an automated sequence. Each line contains 1,024 sampling points axially and 512 points transversally.

The operators ensured that scans were well centered within the acquisition window and that patient fixation was correct. Scan centralization within the acquisition window was done by using the “optimize z-offset” function; if this did not produce adequate centralization, manual correction was performed. If fixation errors were detected, the operator adjusted the fixation point as necessary to ensure the best possible foveal centralization. The “optimize polarization” function was used before acquiring each set of scans to reach the best possible image quality.

After acquisition, we analyzed each scan using the retinal thickness (single eye) protocol to evaluate whether there was any misdetection of the retinal boundaries, seen as a misplacement of the boundary lines. We considered any boundary detection error as an artifact. The number of artifacts and their clinical cause were recorded in each case. Each scan was graded by the same experienced grader (MS).

**Statistical Methods**

To study the factors influencing the number of scans with artifacts, analysis of covariance with forward stepwise variable selection was conducted. Frequency tables and cross-tabulations were used to study the causes of artifacts. Statistical analysis was done by the R system using the Sweave software package (R Development Core Team, Vienna, Austria).⁴

**Results**

The automatic retinal thickness analysis produced reliable determination of the retinal boundaries in 64.7% of eyes, which were considered artifact-free. Artifacts were found in 35.3% of eyes. Distributions of the number of scans affected by artifacts are listed in Table 1, which shows that the majority of eyes with artifacts had only one scan affected by an artifact.

In examining the causes of the artifacts, we found four main reasons: (1) hard exudates; (2) cyst formation; (3) proliferation (fibrovascular proliferative tissue formation); and (4) degraded image quality (eg, due to
cataract). Examples of each type and their typical influence on retinal thickness detection can be seen in Figures 1 to 4.

Artifacts caused by hard exudates represented the majority of artifacts (41.5%), followed by cystoid macular edema (31.7%) and proliferation (17.0%). Artifacts due to other causes represented a smaller proportion than this. The causes of artifacts and the corresponding frequencies are summarized in Table 2. Data showing the number of scans with artifacts in relation to the cause of the artifact are provided in Table 3.

It should be noted that the mean values in the rightmost column of Table 3 do not give the average number of scans with artifacts in the various disease conditions (eg, proliferation), but rather the average number of scans with artifacts if there was at least one artifact.

**Regression Modelling of the Number of Artifacts**

Gender, age of the patient, cause of artifact, and identity of the operator performing the measurement were all recorded, documented, and included in the model. Age was not included during the variable-selection procedure and gender and operator identity showed nonsignificant relationships. However, the number of scans with artifacts was highly dependent on the cause of the artifact, giving $P < .0001 (P = 3.2 \times 10^{-26})$. Residual analysis showed only minor deviation from the normal distribution.

**DISCUSSION**

Quantitative measurement of macular thickness is of great interest in disorders such as diabetic retinopathy. Macular thickness measurements, which are not available using standard examination methods (ophthalmoscopy, fluorescein angiography, or stereoscopic fundus photography), can provide valuable information on disease progression or the effects of treatment. OCT is an ideal candidate for these types of measurements and is widely used for research investigations. Automated measurements and calculations are pre-

**Table 1** Distribution of Artifacts

<table>
<thead>
<tr>
<th>No. of Scans With Artifacts</th>
<th>No. of Eyes</th>
<th>Relative Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (artifact-free)</td>
<td>75</td>
<td>64.7%</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>19.8%</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>4.3%</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>6.0%</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>2.6%</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

**Figure 1.** Typical appearance of a scan of an eye with hard exudates. Note the misdetection of the inner retinal boundary (marked with white arrows).

**Figure 2.** Appearance of a scan of an eye with severe cystoid edema. The base of the cyst was misdetected as the inner retinal boundary (marked with white arrows).
ferred because they exclude the “human factor” from the analysis and in principle should therefore enhance reliability.

However, our results underline the weaknesses of the currently available instrument and its software; it works well with relatively healthy eyes, but in more severe cases of diabetic macular edema the result may be unreliable and less precise than is required for scientific purposes. We found boundary detection errors produced by OCT in randomly selected patients with diabetic retinopathy in 35.3% of the eyes tested. Moreover, these artifacts were not produced because of technical failures, but rather by misdetection of retinal boundaries by the software.

The largest number of artifacts in our study were those produced because of hard exudates. Hard exudates are represented on OCT images as particles of various sizes and of high optical reflectivity situated between the retinal layers. Their presence causes the method used for automatic detection of the retinal boundaries to produce erroneous results.

Cyst formation in diabetic macular edema produces artifacts because the outer boundary of the cyst protrudes above the level of the surrounding retina; the outer reti-

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**TABLE 2**

Frequencies of Artifacts According to Their Different Causes

<table>
<thead>
<tr>
<th>Cause</th>
<th>No. of Eyes Affected</th>
<th>Frequency Among All Eyes (%)</th>
<th>Frequency Among Eyes With Artifacts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artifact free</td>
<td>75</td>
<td>64.7</td>
<td>–</td>
</tr>
<tr>
<td>Exudates</td>
<td>17</td>
<td>14.7</td>
<td>41.5</td>
</tr>
<tr>
<td>Cyst formation</td>
<td>13</td>
<td>11.2</td>
<td>31.7</td>
</tr>
<tr>
<td>Proliferation</td>
<td>7</td>
<td>6.0</td>
<td>17.0</td>
</tr>
<tr>
<td>Degraded image quality</td>
<td>4</td>
<td>3.4</td>
<td>9.8</td>
</tr>
</tbody>
</table>

*Frequencies are shown relative to all eyes (N = 116) and as a percentage of the eyes with artifacts (n = 41).
nal boundary is consequently often incorrectly placed on the boundary of the cyst. Similarly, fibrovascular proliferation is represented on OCT images as an additional tissue layer with high reflectivity above or on the outer retinal boundary; therefore, the outer retinal boundary is often incorrectly placed on the proliferation.

Ray et al.\textsuperscript{5} distinguished six types of image artifacts: inner retinal misidentification, outer retinal misidentification, out-of-register artifacts, degraded image artifacts, cut-edge artifacts, and “off-center” artifacts. As pointed out by Hee,\textsuperscript{6} three of these six types (out-of-register, cut-edge, and “off-center” artifacts) can be avoided by the operator. During grading, we observed only artifacts produced by misidentification of the retinal boundaries (inner retinal misidentification and outer retinal misidentification) and degraded image quality. The other types of artifacts mentioned above were seen during image acquisition, but they were recognized by the operator and the images including such artifacts were rejected and not saved.

Sadda et al.\textsuperscript{7} concluded that errors in the detection of retinal boundaries and in the measurement of retinal thickness are frequent with existing OCT analysis software. They also found that errors were more severe in eyes where subretinal fluid was present. However, due to the nature of the diabetic retinopathy, we did not register any artifacts caused by subretinal fluid in the current investigation.

Somfai et al.\textsuperscript{8} examined artifacts caused by defocusing, depolarization, decentralition, and a combination of defocusing and depolarization. They showed that defocusing and depolarization errors together had the greatest altering effect on all measurements and on segmentation accuracy.

Karam et al.\textsuperscript{9} examined patients with retinal pigment epithelium detachment and retinal laser scars and concluded that lesions that cause disruption of external reflectivity (retinal pigment epithelium) can cause software-related artifacts if analysis protocols are applied.

Suggested Techniques for Reducing the Number of Artifacts

An adequate level of operator experience is the first step for gaining artifact-free images, but even then artifact production is unavoidable in many cases. The macular thickness acquisition protocol allows an opportunity for the operator to reacquire scans during the scanning process, and by this means one can reduce the likelihood of recording artifacts caused by technical factors.

When performing quantitative analysis of retinal mapping data, results always need to be checked for possible artifacts. This check can be done conveniently by verifying the scans one-by-one with the retinal thickness (single eye) analysis protocol because this shows the retinal boundaries the software has detected in each scan separately. If one does find boundary detection errors, acquisition can be repeated in the hope of obtaining fewer errors.

If artifact-free image production fails despite one’s best efforts then, as Sadda et al.\textsuperscript{7} have also pointed out, it is still possible to use the OCT electronic caliper for thickness measurements. However, accurate volume data will not be available in these cases. In addition, manual correction in some situations might unfortunately be poorly reproducible and such ad-hoc alterations would reduce the valid-

<table>
<thead>
<tr>
<th>Cause</th>
<th>No. of Eyes</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artifact free</td>
<td>75</td>
<td>75</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Exudates</td>
<td>17</td>
<td>0</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2.00</td>
</tr>
<tr>
<td>Cyst formation</td>
<td>13</td>
<td>0</td>
<td>10</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.38</td>
</tr>
<tr>
<td>Proliferation</td>
<td>7</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3.71</td>
</tr>
<tr>
<td>Degraded image quality</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.75</td>
</tr>
<tr>
<td>Total</td>
<td>116</td>
<td>75</td>
<td>23</td>
<td>5</td>
<td>7</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>0.73</td>
</tr>
</tbody>
</table>

**TABLE 3**

Cross-tabulation of the Number of Scans With Artifacts According to the Cause of the Artifact and Mean Number of Scans With Artifacts
ity of quantitative results. We also need to add that if automatic measurement fails, manual evaluation is still the gold standard in determining retinal thickness.

To prevent diagnostic errors, as Karam et al. suggest, it is advisable to reevaluate the clinical fundus examination in any patient in whom OCT findings do not appear consistent with the initial clinical findings.

One limitation of our study was that the type of retinal pathology was only registered in cases where artifacts were found in the analysis. Systematic correlation of the retinal status and the OCT images was not performed. For future prospective studies, we recommend registering the conditions that may possibly cause artifacts, even when they do not actually cause an artifact in the image of the examined eye.

In our study, we found that boundary detection errors on OCT images in cases of diabetic retinopathy are frequent occurrences and, therefore, careful checking of quantitative measurements is strongly recommended.

REFERENCES
