Identifying the Boundaries of Retinal Pigment Epithelial Detachments Using Two Spectral-Domain Optical Coherence Tomography Instruments

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BACKGROUND AND OBJECTIVE: To compare two spectral-domain optical coherence tomography (SD-OCT) instruments in identifying the boundaries of retinal pigment epithelium detachment (PED).

PATIENTS AND METHODS: 27 eyes were scanned with Cirrus and Spectralis SD-OCT instruments during a single visit. Two Cirrus scan patterns were used: the 512 × 128 and 200 × 200 covering a 6 × 6 mm (20° × 20°) area. The Spectralis scan pattern consisted of seven B-scans, averaged 51 times, covering a 30° × 5° area. The main outcome measures were the retinal thickness at the foveal center and the number of segmentation failures on the central B-scan.

RESULTS: The Spectralis algorithm failed to follow the proper retinal contour in 25 eyes (92.6%), while the segmentation on the Cirrus instrument was successful in every central B-scan. Spectralis yielded greater retinal thickness measurements in all cases, and the average difference between Cirrus and Spectralis was 139 µm (P < .001). The intraclass correlation coefficient between the two Cirrus scan patterns was 0.998, and Cirrus versus Spectralis was 0.21.

CONCLUSIONS: The Cirrus SD-OCT instrument identifies the appropriate segmentation boundaries in the presence PED. The Spectralis SD-OCT algorithm was unreliable in segmenting PEDs, leading to inaccurate retinal thickness measurements unless manual adjustments were performed.


INTRODUCTION

Retinal pigment epithelium detachments (PEDs) have been associated most commonly with age-related macular degeneration (AMD), central serous chorioretinopathy, and polypoidal choroidal vasculopathy.1 Historically, the diagnosis and follow-up of PEDs were based on imaging with fluorescein angiography (FA) and indocyanine green angiography (ICGA). More recently, optical coherence tomography (OCT) has proven useful for identifying and following PEDs.1,2

The introduction of spectral-domain OCT (SD-OCT) instruments with high scanning speeds and dense scanning patterns covering a large retinal area has eliminated the need to interpolate between just six scans in time-domain technology and has led to a more reliable assessment of retinal thickness measurements.3-6 However, the accuracy of any retinal thickness measurement depends primarily on the accuracy of the segmentation algorithms that identify the retinal boundaries, which include the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE). The currently available SD-OCT instruments each use a different proprietary algorithm. Several papers have recently analyzed various characteristics of these segmentation algorithms,7,8 particularly their reproducibility in a number of different conditions.9-16

The presence of a PED can present a challenge for a segmentation algorithm due to the deformation of the RPE.8,17 Accurate identification of the RPE layer is required to obtain an accurate retinal thickness measurement in the setting of PEDs.13,18 The impor-
tance of accurate and reproducible assessment of retinal thickness is apparent with the use of inhibitors of vascular endothelial growth factor (VEGF) for the treatment of neovascular AMD. A change in the retinal thickness measurement along with qualitative assessment of the B-scans is often used to determine re-treatment in eyes undergoing anti-VEGF therapy, and vascularized PEDs are often a component of the neovascular lesions.19-22 Due to the importance of retinal thickness measurements in the presence of PEDs when re-treating patients with anti-VEGF therapy and when recruiting patients with neovascular AMD into clinical studies, we evaluated the segmentation performance of two SD-OCT instruments, the Cirrus SD-OCT (Carl Zeiss Meditec, Dublin, CA) and the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) in patients with PEDs.

**METHODS**

This prospective study was approved by the institutional review board of the University of Miami Miller School of Medicine and was compliant with the Health Insurance Portability and Accountability Act of 1996. Consecutive patients with a clinical diagnosis of PED affecting the fovea were recruited from the retina service at the Bascom Palmer Eye Institute. All patients signed a research consent form after a detailed explanation of the study.

The Bascom Palmer Eye Institute retina faculty confirmed the clinical diagnosis of a PED. Serous (vascular and nonvascular) and fibrovascular PEDs were included in this study. Digital color fundus imaging, Cirrus SD-OCT imaging, and Spectralis SD-OCT imaging were performed in all patients, and FA and ICGA were ordered according to clinical need.

Eyes with serous PEDs were identified ophthalmoscopically by the presence of a circumscribed and translucent RPE detachment. FA, when available, demonstrated an early hyperfluorescence, which developed into a homogenous hyperfluorescent area with well-defined borders during the late phase.1,23 A serous PED on SD-OCT had a dome-shaped RPE elevation that appeared optically empty. The serous vascularized PEDs on SD-OCT had a dome-shaped elevation of the RPE associated with subretinal or intraretinal fluid, as well as an area of hyperfluorescence, either as a hot spot or plaque seen on ICG angiography.24 Fibrovascular PEDs presented as an RPE elevation with nonhomogenous hyper-reflective material below the RPE layer and overlying or adjacent intraretinal and/or subretinal fluid on SD-OCT imaging. FA revealed early stippled hyperfluorescence associated with late leakage.1

Patients with other retinal pathologies were excluded. Other major exclusion criteria included PEDs too large to fit within the 6 x 6 mm² scanning area, PEDs touching the edge of the scan, and PEDs associated with disciform scars and areas of geographic atrophy.

Each patient was imaged using both SD-OCT instruments on the same day. Each eye was imaged using two raster scan protocols available on the Cirrus...
SD-OCT instrument: 200 × 200 and 512 × 128 A-scans. The 200 × 200 protocol consisted of 200 B-scans, each containing 200 A-scans. This is a homogeneous sample grid with A-scans 30 µm apart. The 512 × 128 protocol consists of 128 B-scans approximately 47 µm apart. The length of each B-scan is 6 mm. On the Spectralis OCT, a scan pattern was chosen that consisted of 7 B-scans, each averaged 51 times, covering a 30° × 5° area. The length of each B-scan was 9 mm. The operator assessed the quality of the scan during its acquisition and, whenever possible, an effort was made to delete datasets with poor signal strength or with significant motion artifacts. The patient was repositioned during the scanning session as necessary, but there was no specific requirement to reset the patient or the instrument after acquiring each dataset.

The main outcome measure was to compare the segmentation performance on the B-scan that included the foveal center. For the Spectralis OCT, the automatic central retinal thickness measurement was ob-
tained from the B-scan through the fovea. The foveal B-scans were then selected from the 200 × 200 or 512 × 128 cube obtained from the Cirrus SD-OCT. Retinal thickness, ie, the distance between the automated segmentations of the ILM and the RPE, was measured manually at the center of the B-scan. A retinal specialist (FP) examined all the scans and evaluated the quality of the segmentation. A segmentation failure was defined as a failure to follow the appropriate retinal boundaries along at least 5% of the B-scan length.

Bland-Altman plots were used to evaluate the agreement of the central retinal thickness measurements between the two SD-OCT instruments (Cirrus: 200 × 200 and 512 × 128 vs. Spectralis) and the two Cirrus acquisition protocols (200 × 200 and 512 × 128). All statistical calculations were carried out with the SPSS V16.0 software (SPSS Inc., Chicago, IL).

RESULTS

Twenty-seven eyes of 25 patients with different types of PEDs were enrolled. The sample included five men and 20 women with a mean age of 68.94 years (range: 51 to 89 years, SD: 8.43). Six eyes (22.23%) were classified as serous nonvascularized PEDs (Fig. 1), 10 eyes (37.03%) as serous vascularized PED (Fig. 2), and 11 eyes (40.74%) as fibrovascular PEDs (Fig. 3).

There are well-known differences between the segmentation algorithms on the two instruments, particularly regarding the location of the RPE boundary. The Cirrus segmentation algorithm placed the RPE boundary line just below the front edge of the hyper-reflective band interpreted as the anatomical RPE. The Spectralis OCT typically segmented the back edge of the same hyper-reflective band, leading to somewhat thicker retinal thickness measurements.13 However, the Spectralis algorithm failed to properly segment the central B-scan in 25 eyes (92.6%). In 20 of these eyes, the algorithm followed Bruch’s
membrane instead of the RPE (Fig. 1). In the remaining five eyes, the segmentation errors were of a more complex nature, as shown in Figures 2 and 3. Figure 4 illustrates a case in which the Spectralis RPE segmentation was judged successful. The Cirrus instrument correctly segmented the RPE layer in every central B-scan.

The mean center point thickness recorded by the Spectralis was 362.29 µm ± 156.37 µm (176-919 µm). The mean center point thickness using the Cirrus was 220.18 µm ± 69.30 µm (119-393 µm) and 223.33 µm ± 70.04 µm (119-399 µm), using the 200 × 200 or 512 × 128 scan patterns, respectively. There was a small (3 µm) but statistically significant difference between the two Cirrus scan patterns (P = .012) (Fig. 5). There was a large and significant difference between the Cirrus and the Spectralis central retinal thickness measurements (P < .001). The average difference between Cirrus 512 × 128 versus Spectralis was 139 µm (SD: 140) and Cirrus 200 × 200 versus Spectralis was 136 µm (SD: 137), with consistently larger measurements for the Spectralis instrument. The intraclass correlation between the two Cirrus scan patterns was 0.998, and the Cirrus 512 × 128 protocol versus Spectralis was 0.21. The Bland-Altman plot illustrates this important systematic difference, showing a greater disagreement between the instruments for larger lesions (Fig. 6).

**DISCUSSION**

Both time-domain OCT and SD-OCT can provide very reproducible retinal thickness measurements. However, the vast majority of the reproducibility studies with different OCT machines were conducted in healthy subjects. A study compared the measurements of central retinal thickness using seven OCT devices in patients without retinal diseases. Not surprisingly, the mean CRT was similar using Spectralis and Cirrus SD-OCT but not identical, with a difference of 20 µm. Giani et al. conducted a study that evaluated retinal thickness measurements using six OCT devices, including both normal and pathologic eyes. They concluded that retinal thickness measurements are different between the instruments due to differences in the algorithm analysis. The greatest difference was 175 µm between SD-OCT Copernicus HR (Optopol Technology SA, Zawiercie, Poland) and Spectralis, because Copernicus identifies the outer boundary as the inner edge of the RPE complex.

While there are known differences between the instruments based on the location of the RPE segmentation boundary in normal retinas, the true test of an algorithm is its ability to follow a boundary when the normal anatomy is disturbed. Imaging neovascular AMD patients with SD-OCT can be challenging, especially when there is complex anatomy and the retinal thickness measurements are needed for deciding when to re-treat with anti-VEGF therapy or for use in recruitment or as an endpoint in clinical trials. The present research compared the central retinal thickness measurements (on a single B-scan) in patients with PEDs associated with wet AMD using two common SD-OCT commercial instruments. This study was performed to simulate a standard clinical situation faced by physicians when monitoring these.

![Figure 6. Bland-Altman plot comparing the central retinal thickness (CRT) measurements at the central B-scan by Cirrus and Spectralis machine. The solid line represents the average difference, which is about 139 µm. All points are above zero, showing that the Spectralis CRT values are consistently greater than the Cirrus measurements. (A) Represents Cirrus 200 × 200 scan pattern versus Spectralis. (B) Represents Cirrus 512 × 128 scan pattern versus Spectralis.](image-url)
types of patients. Typically, patients with PEDs are monitored by SD-OCT, and qualitative as well as quantitative changes in anatomy, such as the status of macular fluid and central retinal thickness, are followed. The retinal thickness is a meaningful clinical parameter only if the underlying segmentation accurately reflects the anatomical condition. The results of the present paper suggest that the Cirrus SD-OCT algorithm is significantly more accurate than the Spectralis SD-OCT algorithm in the presence of a PED.

The Spectralis SD-OCT algorithm produces slightly larger retinal thickness measurements than the Cirrus SD-OCT when both RPE segmentations follow the RPE layer in a normal macula; however, in the presence of PED, the difference in retinal thickness measurements differs dramatically because the Spectralis algorithm fails to follow the RPE layer. Moreover, our study shows that the segmentation algorithm on the Spectralis instrument does not behave consistently with respect to the choice of the outer boundary. While it followed Bruch’s membrane in most cases, there were five eyes in which the Spectralis algorithm attempted to follow the RPE layer but failed and two eyes in which it actually followed the RPE anatomy correctly.

In summary, the Cirrus SD-OCT algorithm identifies the appropriate retinal boundaries in the presence of PEDs and provides accurate retinal thickness measurements. The Spectralis SD-OCT algorithm is inconsistent when segmenting PEDs, producing inaccurate retinal thickness measurements that require manual adjustment. It is always important to check whether the automated segmentation is correct before accepting the retinal thickness measurements on any instrument, but this is particularly true when using the Spectralis OCT to image eyes with PED.