Macular Thickness Measurements in Normal Eyes Using Spectral Domain Optical Coherence Tomography

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BACKGROUND AND OBJECTIVE: Knowledge of the macular thickness in a normal population is important for the evaluation of pathological macular change. The purpose of this study was to define and measure macular thickness in normal eyes using spectral domain optical coherence tomography (OCT).

PATIENTS AND METHODS: Fifty eyes from 50 normal subjects (29 men and 21 women, aged 22 to 68 years) were scanned with a prototype Cirrus HD-OCT system (5 µm axial resolution) (Carl Zeiss Meditec, Inc.). The proprietary Cirrus segmentation algorithm was used to produce retinal thickness maps, which were then averaged over 9 regions defined by a circular target centered at the true fovea location. The macular thickness of 13 subjects scanned with both HD-OCT and StratusOCT were compared.

RESULTS: After centering the fovea, the mean and standard deviation values for retinal thickness measurements were calculated point wise and averaged on standard regions. For patients scanned with both systems, the thickness measurements from HD-OCT were approximately 50 µm larger than those from StratusOCT. The difference between the two measurements decreased somewhat with eccentricity.

CONCLUSION: Using HD-OCT, it is possible to acquire retinal data sets containing an unprecedented number of data points. Furthermore, it is possible to use OCT fundus images to evaluate the scan quality and to center the measurement at the fovea. These advantages, together with good automated segmentation, can produce more accurate retinal thickness measurements. Incorporation of the photoreceptor layer in the measurements is anatomically meaningful and may be significant in evaluating various retinal pathologies and visual acuity outcomes.

INTRODUCTION

Because macular thickness has been found to significantly correlate with visual acuity,¹ knowledge of normal population thickness would be essential for studying and evaluating macular thickening due to various ocular pathologies. Optical coherence tomography (OCT) is a noninvasive technology that enables clinicians to detect and monitor subtle changes in macular thickening.²⁻⁷ Several studies have reported normative macular thickness data obtained using the StratusOCT (Carl Zeiss Meditec, Inc., Dublin, CA) commercial system.⁸⁻⁹
Recent advances in OCT technology have led to the development of faster, more sensitive OCT scanning systems, known as spectral domain OCT (SD-OCT). SD-OCT systems are capable of acquiring large, volumetric data sets in a short time frame. Several commercial versions of SD-OCT instruments are currently entering the marketplace. For the current study, we used a prototype Cirrus HD-OCT instrument from Carl Zeiss Meditec, Inc. that has an axial resolution of approximately 5 µm and is capable of acquiring approximately 27,000 A-scans per second. Compared to StratusOCT, where six 6-mm B-scans are acquired in a radial pattern centered on the patient’s fixation point, HD-OCT can acquire up to 200 six-mm B-scans in a cube pattern centered on the patient’s fixation point or an operator-selected point in one scan set (Fig. 1).

One important feature of SD-OCT raster scans is that fundus-like images can be reconstructed from the data sets. These OCT fundus images can be obtained as soon as the scan is acquired and serve as a useful tool for screening the image quality by determining whether eye movements occurred during the scan. B-scans are automatically registered to the fundus-like images, allowing for accurate spatial correlations of the SD-OCT images (Fig. 2). These capabilities solve the greatest problems associated with StratusOCT retinal thickness maps: the lack of precise correspondence between the B-scans and the retinal topography, the difficulties accounting for eye motions, and the substantial need for data interpolation. Unstable fixation and imprecise targeting can lead to inaccuracies in calculating retinal thickness measurements.

The SD-OCT volumetric data set can be analyzed using specialized segmentation algorithms that automatically identify the boundaries between specific retinal layers. This information can be used to generate surface maps and thickness maps of the retina. The maps can be used for qualitative and quantitative analysis (Fig. 2).

With the increasing use of SD-OCT by ophthalmologists, it would be critical to measure macular thickness in healthy individuals, not only to provide normative data, but also to compare these values with the current OCT system. The purpose of this study was to define and measure macular thickness in normal eyes using the Cirrus HD-OCT system.

**PATIENTS AND METHODS**

A prospective study was performed at Bascom Palmer Eye Institute after approval from the institutional review board at the University of Miami was obtained. This study was compliant with the Health Insurance Portability and Accountability Act of 1996. A written informed consent was administered to all subjects before any research scans were obtained.

Fifty pairs of eyes from 50 normal subjects were scanned with the Cirrus HD-OCT. For this study, we used a scan pattern composed of 200 × 200 A-scans (the second factor denotes the number of B-scans, the first factor denotes the number of A-scans per B-scan), which covers uniformly a 6 × 6 mm square on the retina. The depth of each scan is 2 mm. Each subject had both eyes scanned during image acquisition. How-
ever, for the purpose of thickness measurements, only the right eye of each participant was included.

Of the subjects, 29 were men and 21 were women. Their ages ranged between 20 and 68 years. Subjects were excluded from the study if they had any known ocular disease. After image acquisition, two retina specialists carefully reviewed these scans for abnormalities. Thirteen individuals (selected randomly) were also scanned with StratusOCT and the retinal thickness measurements were directly compared to the results on HD-OCT. StratusOCT data were also collected in these eyes using the “radial lines” protocol, which consists of six radial scans with the center approximately on the fovea.

The Cirrus HD-OCT measures macular thickness using a proprietary algorithm developed at the Bascom Palmer Eye Institute by the second author. This algorithm detects the internal limiting membrane as the inner retinal boundary and the anterior surface of the retinal pigment epithelium as the outer retinal boundary. Once the boundaries are segmented, false-color three-dimensional and two-dimensional thickness maps are generated. Macular thickness measurements were obtained in nine regions, which were similar to those in the Early Treatment Diabetic Retinopathy Study. The central circle has a diameter of 1 mm. The inner circle has a diameter of 3 mm and is divided into four quadrants. The outer circle has a diameter of 6 mm and is also divided into four quadrants. Thickness values obtained from retinal segmentation are averaged to give the mean thickness in each quadrant.

One of the major advantages of the SD-OCT technology is that retinal features can be localized precisely in the OCT data set a posteriori. This means that it is not necessary to rely on the patient’s ability to fixate or the operator’s ability to center a scan properly. To obtain optimal thickness measurements, the first author reviewed each data set and localized the true fovea position. These coordinates were used to determine the center of the measurements region for the two-dimensional thickness map.

The StratusOCT mapping software was used to create a two-dimensional retinal thickness map for

**TABLE 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HD-OCT</th>
<th>StratusOCTa</th>
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<tbody>
<tr>
<td>Fovea (500 µm)</td>
<td>258.2 ± 23.5</td>
<td>212 ± 20</td>
</tr>
<tr>
<td>Inner ring (1.5-mm radius)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior</td>
<td>326.6 ± 18.9</td>
<td>255 ± 17</td>
</tr>
<tr>
<td>Inferior</td>
<td>326.0 ± 24.4</td>
<td>260 ± 15</td>
</tr>
<tr>
<td>Temporal</td>
<td>312.6 ± 17.1</td>
<td>251 ± 13</td>
</tr>
<tr>
<td>Nasal</td>
<td>328.6 ± 18.3</td>
<td>267 ± 16</td>
</tr>
<tr>
<td>Outer ring (3-mm radius)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior</td>
<td>282.5 ± 14.9</td>
<td>239 ± 16</td>
</tr>
<tr>
<td>Inferior</td>
<td>270.9 ± 13.9</td>
<td>210 ± 13</td>
</tr>
<tr>
<td>Temporal</td>
<td>266.3 ± 17.7</td>
<td>210 ± 14</td>
</tr>
<tr>
<td>Nasal</td>
<td>295.5 ± 17.0</td>
<td>246 ± 14</td>
</tr>
</tbody>
</table>

OCT = optical coherence tomography.

aAs reported by Chan et al.22

The Cirrus HD-OCT and Stratus OCT systems are manufactured by Carl Zeiss Meditec, Inc., Dublin, CA.
subjects scanned with the machine. These measurements were then correlated with the results obtained with the HD-OCT.

RESULTS

The mean and standard deviation for macular thickness were calculated and tabulated in Table 1. Similar to previous studies, thickness values were lowest in the fovea center. Macular thickness was highest within the 3-mm diameter of the center and the thickness decreased between the 3- to 6-mm diameter outside the center.

StratusOCT scans were also taken of 13 eyes of 13 individuals randomly selected from our population. The mean and standard deviation for macular thickness were calculated and tabulated in Table 2. The results clearly show that the HD-OCT measurements are consistently larger than those obtained with StratusOCT. As we discuss later, this difference was expected and is due to the inclusion of the outer segments of the photoreceptors in the HD-OCT measurements. Although the difference between the two instruments decreases somewhat with eccentricity, the measurements are tightly correlated (Fig. 3).

DISCUSSION

A novel feature of SD-OCT is the ability to generate a reconstructed fundus image by summing along the A-lines. Compared to StratusOCT, where six radial line scans are presumed to be taken in or around the fovea, individual B-scans on HD-OCT are registered to the reconstructed fundus image (Fig. 2), allowing for accurate spatial localization.

The HD-OCT fundus image is also useful for image quality control, allowing for an immediate assessment of any image artifacts or eye movements present in the data set at the time of acquisition. Because of the large num-

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HD-OCT</th>
<th>StratusOCT</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fovea (500 µm)</td>
<td>266.2 ± 22.7</td>
<td>203.9 ± 20.0</td>
<td>62.3 ± 7.3</td>
</tr>
<tr>
<td>Inner ring (3-mm radius)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Superior</td>
<td>327.6 ± 12.7</td>
<td>274.9 ± 14.6</td>
<td>52.7 ± 5.8</td>
</tr>
<tr>
<td>Inferior</td>
<td>324.2 ± 12.8</td>
<td>269.0 ± 15.6</td>
<td>55.2 ± 6.7</td>
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<tr>
<td>Temporal</td>
<td>315.2 ± 14.3</td>
<td>259.4 ± 13.8</td>
<td>55.8 ± 7.8</td>
</tr>
<tr>
<td>Nasal</td>
<td>331.0 ± 12.2</td>
<td>275.2 ± 15.9</td>
<td>55.8 ± 6.8</td>
</tr>
<tr>
<td>Outer ring (6-mm radius)</td>
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<td></td>
</tr>
<tr>
<td>Superior</td>
<td>281.4 ± 11.3</td>
<td>236.0 ± 13.2</td>
<td>45.4 ± 8.3</td>
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<tr>
<td>Inferior</td>
<td>268.3 ± 8.2</td>
<td>216.7 ± 13.9</td>
<td>51.6 ± 9.9</td>
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<tr>
<td>Temporal</td>
<td>263.5 ± 12.2</td>
<td>215.3 ± 10.5</td>
<td>48.2 ± 6.6</td>
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<tr>
<td>Nasal</td>
<td>296.7 ± 11.8</td>
<td>248.9 ± 14.7</td>
<td>47.8 ± 7.5</td>
</tr>
</tbody>
</table>

OCT = optical coherence tomography.
The Cirrus HD-OCT and StratusOCT systems are manufactured by Carl Zeiss Meditec, Inc., Dublin, CA.
The mapping software takes the six radial lines centered on the fovea and spaced 30° apart, interpolates data between the scans, and generates a thickness map. Unfortunately, regardless of the StratusOCT scan protocol (fast vs standard), it is difficult to judge whether the scans actually intersect at the fovea and, if they do not, it is not possible to estimate the error introduced. Eye movements can complicate the matter and they are basically impossible to detect.

The combination of issues affecting image quality with well-known segmentation problems often makes it difficult to judge the accuracy of a StratusOCT thickness map. Even when all of the radial lines perfectly intersect at the fovea, it is necessary to rely on interpolation to estimate the retinal thickness between the scans. The result is a massive loss of detail and is highly dependent on the assumed symmetry of the eye to be correct.

With the large quantity of volumetric data acquired by HD-OCT, the area within the scanning box is uniformly imaged, eliminating the need for interpolation. Retinal thickness maps are more accurate and detailed because they are generated using a much larger set of actual data points. Moreover, scan acquisition is not as dependent on patient fixation because of the large retinal area covered, and the operator can manually move the scan window while looking at the retinal scanning laser ophthalmoscope image. Despite the best efforts of a trained operator, the OCT data sets will often not be centered at the fovea. However, the true position of the fovea in the 6 × 6 mm scanning box can be determined a posteriori examining the data set (Fig. 4).

Because of the uniform sampling over the scan region, the center of the measurement target can be easily moved to the true fovea position. In extreme circumstances, as illustrated in Figure 5 (which is not representative of the data used in this article), manual selection of the fovea position results in the placement of the outer ring of the thickness map outside the range of data points collected in the scanning region. In this case, the result is the average retinal thickness of only the region of the quadrant overlapping the scanning box. Although the accuracy of thickness values in the outer rings may suffer because of centration problems, it should be pointed out that, except in extreme cases, they are still based on considerably more sample points than StratusOCT measurements.

For the scans analyzed in this article, some of the outer ring quadrants could fall outside of the scanning region, but the central retinal thickness and the thickness values for the inner ring quadrants were all properly aligned and fully accounted for in the retinal thickness measurements. Although at this time the Cirrus HD-OCT algorithm has not been independently validated, the authors checked the results on the data sets presented here and no recognizable errors were found.

It should be stressed again that the software we used selects a different outer boundary for the calculation of retinal thickness than StratusOCT. In StratusOCT, the segmentation mapping software selects the inner segment/outer segment (IS/OS) junction as the outer retinal boundary. Our HD-OCT segmentation algorithm selects the inner boundary of the retinal pigment epithelium layer as the outer retinal boundary (Fig. 5).

This difference allows our HD-OCT measurements to incorporate the full thickness of the photoreceptor layer in macular thickness measurements. This difference will, of course, give rise to larger retinal measurements from the HD-OCT algorithm. More importantly, our measurements are more meaningful from an anatomical point of view because the retinal pigment epithelium is a more stable marker than the IS/OS junction. Furthermore, including the thickness of the photoreceptor layer in retinal thickness measurements could be useful when comparing normal and pathological eyes with photoreceptor layer disruption.

Our results show that macular thickness in HD-OCT was approximately 50 µm thicker than the corresponding StratusOCT values because of the inclusion of the photoreceptor layer in the measurements (Tables 1 and 2). It should also be noted that the difference between HD-OCT and StratusOCT measurements decreases somewhat as we move away from the fovea. This is consistent with published measurements of the length of the photoreceptors’ outer segments.
The eccentricity effect is fairly small and the measurements on the two instruments are highly correlated (Fig. 3) when considered in their totality. In first approximation, it could be concluded that a conversion factor of approximately 50 µm could be applied to compare the two sets of measurements.

When dealing with macular thickness measurements, an accurate boundary selection is important for accurate thickness values. Poor image quality can lead to algorithm failures. The HD-OCT allows for an immediate assessment of image quality, and the higher resolution should enable algorithms to more...
accurately detect retinal boundaries. The amount of data in HD-OCT images leads to more accurate and detailed macular thickness maps. The ability to center the measurements accurately on the true fovea should reduce the variance of a normative database and therefore allow for better comparisons, both dynamically on a given patient and cross-sectionally over a population. This may prove to be useful in comparing and following thickness measurements in patients having macular disease.

REFERENCES