Effect of Eccentric and Inconsistent Fixation on Retinal Optical Coherence Tomography Measures

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**Objective:** To assess the relative stabilities of optical coherence tomography (OCT)–based retinal volume and central foveal thickness measurements in the setting of eccentric or inconsistent fixation.

**Methods:** Ten healthy right eyes underwent multiple macular OCT centered at fixation. To model the effect of eccentric or inconsistent fixation, OCT was repeated with scan centers precisely shifted by 0.50, 1.00, and 1.50 mm in each of 4 directions. At each scan location, retinal volumes within a series of radii of the scan center, as well as central foveal thickness, were calculated. The main outcome measure was the percentage effect of decentered scanning on each OCT-based variable.

**Results:** Central foveal thickness was the variable most affected in this model of eccentric and inconsistent fixation. This variable demonstrated changes from baseline-centered scans of up to 69.4%. Retinal volumes within a radius of the scan center measuring 1.11 mm or greater were least affected by decentered scanning, demonstrating maximum changes from baseline-centered scans of only 15.7% ($P<.001$ vs foveal thickness).

**Conclusion:** Optical coherence tomography–based retinal volume quantification provides a more stable measure than foveal thickness in the setting of eccentric or inconsistent fixation as may occur in the setting of macular pathologic conditions.

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Many pathologic processes result in retinal edema, and quantification of this process is of great clinical importance. Optical coherence tomography (OCT) is capable of measuring retinal thickness to within approximately 10 to 14 µm, making it a valuable clinical tool. However, technologies that are highly precise under ideal conditions and during short periods may be subject to large long-term fluctuations because of operator and subject factors. These short- and long-term variabilities are somewhat analogous to the short- and long-term fluctuations associated with visual fields. Although it has been well established that OCT–based retinal thickness determinations are subject to small intrasession and short-term intersession variabilities, long-term variability may be a more important issue for patients undergoing successive OCT examinations. To date, factors affecting the long-term fluctuation of successive OCT test results have not been well explored.

One potentially important source of long-term variability in OCT–based measures is eccentric fixation and, in particular, fixation that varies between examinations. Indeed, some patients with diabetic macular edema exhibit eccentric fixation that shifts location over time. By using significantly more of the available OCT–generated information, retinal volume measures may be less susceptible to changes resulting from such inconsistent fixation. This may be of importance during long-term follow-up with successive measurements. However, it is unknown which retinal region generates volume measures that are least affected by changes in fixation and how this compares with commonly used foveal thickness measurements. Therefore, we simulated variable fixation using precisely decentered OCT and evaluated the effect on OCT–based retinal volume and foveal thickness measurements.

**METHODS**

The technological specifics of OCT have been described previously. In the present study, OCT was carried out using a commercially available system (StratusOCT 3.0 model 3000; Carl Zeiss Meditec, Dublin, Calif). Using an internal fixation target, a total of 160 scans were...
performed on the undilated right eyes of 10 healthy subjects. In each subject, 4 scans were first carried out centered at fixation. Next, to simulate altered and eccentric fixation, scans were carried out centered at 12 eccentric locations. These locations were located superior, nasal, inferior, and temporal to the point of fixation at distances of 0.50, 1.00, and 1.50 mm. The sample size was chosen to provide an estimated power of 90% to detect a difference of 10% in the effect of altered fixation among the variables investigated at \( \alpha = 0.01 \).

A fast macular thickness protocol was used throughout all studies on all subjects. This protocol provides A-scans at a total of 768 points equally spaced along six 6-mm-long radial lines intersecting at their midpoints. The StratusOCT software algorithm was used to define the internal limiting membrane and the retinal pigment epithelium. All 960 individual line scans were manually reviewed to verify that the algorithm had accurately identified these structures. Retinal thickness at each A-scan location was then determined as the distance between these landmarks. Central foveal thickness, termed foveal thickness in the software algorithm, was calculated as the mean thickness at the intersection of the 6 radial scan lines. Retinal sector volumes were calculated by multiplying the mean thickness by the surface area within the 9 Early Treatment of Diabetic Retinopathy Study sectors (Figure 1). Appropriate retinal sector volumes were summed to provide volume measurements within radii of 0.50, 1.11, 1.50, 1.73, and 3.00 mm of the scan center. The calculation of total retinal volume within radii of 1.11 mm and 1.50 mm required the export of data, as the software algorithm does not automatically provide these measures.

![Figure 1](source_of_figure1) Surface layout of retinal divisions (9 sectors) as generated by optical coherence tomography (Stratus OCT 3.0 model 3000; Carl Zeiss Meditec, Dublin, Calif) (right eye). Output mode 1: A, B, and C were 0.50, 1.11, and 1.73 mm from fixation, respectively. Output mode 2: A, B, and C were 0.50, 1.50, and 3.00 mm from fixation, respectively. I indicates inferior; N, nasal; S, superior; and T, temporal.

![Table](source_of_table) Table. Retinal Volume and Foveal Thickness Measures Under Centered and Decentered Optical Coherence Tomographic Conditions*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Centered Scan</th>
<th>0.50</th>
<th>1.00</th>
<th>1.50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal volume, mm(^3)</td>
<td>0.162 (0.154-0.169)</td>
<td>0.191 (0.183-0.198)(\dagger)</td>
<td>0.217 (0.209-0.224)(\dagger)</td>
<td>0.210 (0.203-0.218)(\dagger)</td>
</tr>
<tr>
<td>0.50-mm Radius</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.11-mm Radius</td>
<td>1.00 (0.97-1.04)</td>
<td>1.01 (0.98-1.04)</td>
<td>1.02 (0.98-1.05)</td>
<td>1.00 (0.97-1.04)</td>
</tr>
<tr>
<td>1.50-mm Radius</td>
<td>1.73 (1.67-1.79)</td>
<td>1.68 (1.63-1.73)</td>
<td>1.60 (1.55-1.66)</td>
<td>1.56 (1.50-1.61)</td>
</tr>
<tr>
<td>1.73-mm Radius</td>
<td>2.51 (2.42-2.59)</td>
<td>2.47 (2.40-2.55)</td>
<td>2.39 (2.31-2.47)</td>
<td>2.31 (2.24-2.40)</td>
</tr>
<tr>
<td>3.00-mm Radius</td>
<td>6.95 (6.74-7.15)</td>
<td>6.92 (6.73-7.12)</td>
<td>6.90 (6.68-7.11)</td>
<td>6.79 (6.53-7.05)</td>
</tr>
<tr>
<td>Foveal thickness, µm</td>
<td>167 (158-178)</td>
<td>240 (230-250)(\dagger)</td>
<td>280 (269-291)(\dagger)</td>
<td>268 (258-278)(\dagger)</td>
</tr>
</tbody>
</table>

*Data are given as mean (95% confidence intervals). The optical coherence tomography was performed using the Stratus OCT 3.0 model 3000 (Carl Zeiss Meditec, Dublin, Calif).

\(\dagger\)P < .001, decentered vs centered.

\(\ddagger\)P < .01, decentered vs centered.

Paired t tests were used for comparisons of individual variables under eccentric and central fixation conditions. The percentage changes in OCT measures induced by alterations in fixation were compared between variables using unpaired t tests. Finally, Wilcoxon rank sum tests were used for comparisons in which sample size required the use of nonparametric testing.

The direction of decentration did not significantly affect the magnitude of the error induced (\(P > .20\) for all comparisons, Wilcoxon rank sum test). Therefore, to maximize generalizability, scans of equal decentration distance were grouped in subsequent analyses. Eccentric scanning resulted in significant changes in foveal thickness measurements regardless of the amount of eccentricity (Table and Figure 2). Retinal volume within the smallest radius, 0.50 mm, also exhibited a mean value that was significantly affected by all degrees of decentralization. In contrast, retinal volume measures within larger radii were affected to a lesser extent. The mean retinal volume within a 1.73-mm radius was significantly affected only when decentration reached 1.50 mm, while the mean volumes within other radii were not significantly altered by decentered scanning.

To overcome the potential for comparisons of mean values to misinterpret changes of equal magnitude but of opposite direction, results were further assessed by comparing the percentage changes in values with decentered scanning. On this percentage basis, foveal thickness was again affected to a much larger extent than any of the retinal volume variables. Foveal thickness measures were in error by 44.5%, 69.4%, and 62.1% with 0.50, 1.00, and 1.50 mm of decentralization, respectively. Although all retinal volume variables were more stable than foveal thickness, the volume within a 0.50-mm radius of the scan center was altered by decentered scanning to the greatest extent, with the change reaching up to 34.7%. This was significantly greater than the changes induced in retinal volumes within larger radii which reached a maximum value of 15.7% (\(P < .01\) for all comparisons). The effect of decentralization was not significantly different among the retinal volumes within radii measuring 1.11 to 3.00 mm.
Several studies using different criteria have investigated the repeatability of OCT-based retinal thickness measurements. For example, the coefficient of variation for single-point thickness determinations at the intersection of 6 radial lines through fixation is approximately 5%. However, this represents the intra-session variation among scans carried out at a single sitting in rapid succession. Because the inter-session variability of single-point thickness measurements is larger, the mean thickness determinations within retinal regions have been suggested for clinical use. The intersession coefficient of variation for such mean thickness measurements is larger, the mean thickness determinations within retinal regions have been suggested for clinical use. The intersession coefficient of variation for such mean thickness measurements within 500 μm of fixation is 5% in healthy eyes and 6% in eyes with diabetic macular edema.

These previous studies examined the technological limits of precision under ideal circumstances and during short intervals as opposed to the long-term follow-up periods encountered clinically. In contrast, our study examined the potential for errors in retinal volume and foveal thickness measurements in the setting of decentered scanning as may be encountered during clinical follow-up. To the best of our knowledge, this is the first study to quantify the effect of altered fixation on these variables. In addition, by exporting data, we were able to calculate and assess retinal volumes within radii not yet available from the software algorithm.

The results of our model demonstrate an inverse relationship between the magnitude of the effect of decenteration and the size of the retinal area sampled. Retinal volume measures within the center subfield of the fast macular thickness protocol and foveal thickness measures are particularly vulnerable. However, all retinal volume measurements, including the center subfield, were affected to a lesser degree than foveal thickness determinations. This stability in the face of altered centration may be an asset during the diagnosis and follow-up of patients with macular edema. However, a counterbalancing argument could be made that retinal volume measurements are simply blunt unresponsive measures with a concomitant lack of sensitivity to clinically important degrees of edema. To address this issue, a companion study investigated this possibility and found that retinal volume and foveal thickness variables display comparable sensitivities and specificities in the detection of clinically significant macular edema. Therefore, by providing improved long-term stability while maintaining powerful sensitivities and specificities in the diagnosis of macular edema, central retinal volume measures have the potential to be of great clinical utility.

A possible weakness of our model is the use of healthy eyes, suggesting that the findings may not be generalizable to pathologic conditions. Although further work will be needed to explore this area, we believe that it is reasonable to extrapolate our results to pathologic states, as single-point thickness measures are likely to remain more responsive to alterations in fixation than measures such as retinal volume that rely on multiple points of data for their generation.

Finally, one must consider the clinical relevance of our results. Although the occurrence of eccentric and inconsistent fixation in patients with macular disease is well established, the frequency of such occurrences in the long-term follow-up of patients with macular disease is unknown. Scenarios in which this could become relevant include not only eccentric fixation but also small eye movements during scanning and changes in fixation during long-term follow-up. Although clinicians may be able to identify alterations in fixation by observing the location of the foveal pit on the retinal thickness map, macular pathologic conditions often make the detection of the foveal pit impossible. Alternatively, the use of the landmarking function of commercial OCT systems, while not preventing eccentric fixation, may help in efforts to consistently image the same section of retina during follow-up. In summary, pending the widespread availability of OCT registration and tracking systems, clinicians will need to be cognizant of the potentially important effect of scan centration on OCT-based measurements.

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REFERENCES


Ophthalmological Numismatics

Mauno Vannas (1891-1964) was professor of ophthalmology at the University of Helsinki, Helsinki, Finland. Vannas was a great opportunist and surgeon. The scissors he designed for use in intraocular surgery are popular and used to this day.

In 1971, a medal depicting Vannas was made in honor of his 70th birthday. It was designed by the artist Oskari Jauhiainen. The obverse depicts his bust facing left. The reverse depicts a stylized eye, the sun, and a von Graefe knife.

Courtesy of: Jay M. Galst, MD, 30 E 60th St, New York, NY 10022.