
Inter-Visit and Inter-Instrument Variability for Cirrus HD-OCT Peripapillary Retinal Nerve Fiber Layer Thickness Measurements

M.R. HORNE, T. CALLAN, M. DURBIN, T. ABUNTO

Carl Zeiss Meditec, Inc., Dublin, CA USA

ABSTRACT

PURPOSE: To measure the reproducibility of retinal nerve fiber layer (RNFL) thickness measurements from Cirrus Optical Coherence Tomography (Cirrus™ HD-OCT), and to determine if inter-visit or inter-instrument variability contribute significantly to overall variance. **METHODS:** First, a single operator scanned one eye of fifteen (15) healthy subjects using the Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) Optic Disc 200x200 scan. Subjects were imaged twice per system during a single visit on five systems. Instrument order was randomized for each subject. Then, the same operator scanned one eye of seventeen (17) healthy subjects using the same Optic Disc 200x200 scan three times per visit on three different visits. All scans for both phases were acquired within one week. Seventeen (17) average thickness parameters were calculated, including the average around a circle at 1.73 mm from the optic disc, four quadrant averages and twelve clock-hour RNFL thickness averages. Analysis of variance (ANOVA) was performed on all parameters using a random effects model without interactions. Variance components were used to estimate the reproducibility. **RESULTS:** Neither the inter-visit nor the inter-system component was statistically significant

for any of the parameters. The reproducibility standard deviation (SD) of the average thickness was 1.4 μm . For the quadrants, the reproducibility SD was 2.9 μm Temporal, 5.1 μm Superior, 4.0 μm Nasal, and 4.1 μm Inferior. The clock-hour reproducibility SD ranged from 3.0 μm at 9 o'clock to 9.0 μm at 12 o'clock. **CONCLUSIONS:** We observed no statistically significant inter-visit or inter-system variability. The small random component of variance observed in both experiments corresponds to a high degree of reproducibility for all parameters for Cirrus HD-OCT peripapillary RNFL thickness measurements.

INTRODUCTION

Software version 3.0 for Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) provides new scan and analysis capabilities for glaucoma management. This includes an analysis package for use in clinical practice to measure retinal nerve fiber layer (RNFL) thickness. Good inter-visit reproducibility independent of instrument variability is critical to differentiating between measurement variability and true change. The purpose of this study was to measure the inter-visit and inter-instrument variability of retinal nerve fiber layer (RNFL) thickness in Cirrus HD-OCT.

METHODS

Data Collection for Inter-system Variability

A single operator scanned one eye of fifteen (15) healthy subjects using the Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) Optic Disc 200x200 scan. Subjects were imaged twice per system during a single visit on five systems. Instrument order was randomized for each subject.

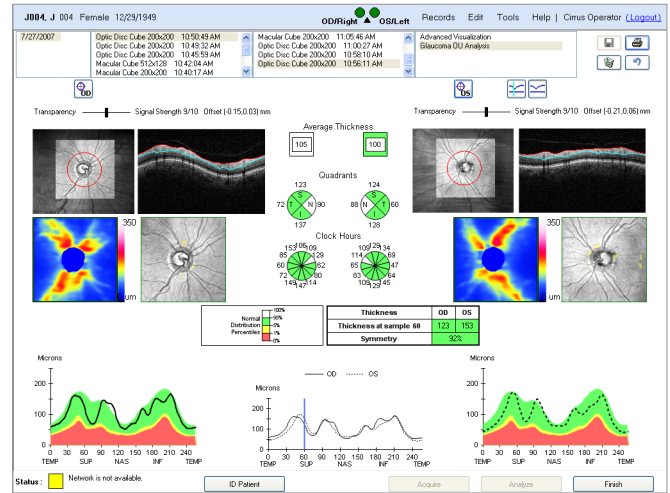
Data Collection for Inter-visit Variability

The same operator scanned one eye of seventeen (17) healthy subjects using the same Optic Disc 200x200 scan three times per visit on three different visits.

Data Analysis for both Studies

All scans for both phases were acquired within one week. Average thickness parameters were calculated, including the average of a circle at 1.73 mm radius from the center of the optic disc, four quadrant averages (temporal, superior, nasal and inferior), and twelve clock-hour RNFL thickness averages. Analysis of variance (ANOVA) was performed on all parameters using a random effects model without interactions. Variance components were used to estimate the reproducibility.

Cirrus Glaucoma Analysis Screen



RESULTS

Descriptive Statistics

Mean thicknesses (and standard deviation) for each system and for each visit are shown in the following tables (see Figures 1-3). For example, the first column, first row of Figure 1 below represents the mean thickness measured on System 1 across all subjects. All units are in microns (μm).

N = 15	Average	Temporal	Superior	Nasal	Inferior
System 1	93 +/- 8	60 +/- 7	118 +/- 14	69 +/- 11	124 +/- 14
System 2	93 +/- 8	60 +/- 8	118 +/- 14	69 +/- 10	124 +/- 14
System 3	92 +/- 8	59 +/- 8	118 +/- 13	70 +/- 10	121 +/- 16
System 4	92 +/- 9	60 +/- 8	117 +/- 14	69 +/- 11	122 +/- 16
System 5	93 +/- 9	60 +/- 8	119 +/- 13	70 +/- 11	122 +/- 16
Visit 1	92 +/- 8	68 +/- 11	117 +/- 13	63 +/- 7	118 +/- 15
Visit 2	92 +/- 7	67 +/- 11	117 +/- 12	63 +/- 7	119 +/- 15
Visit 3	92 +/- 7	67 +/- 11	117 +/- 12	63 +/- 6	118 +/- 14

Figure 1

Analysis of Variance

Subject, instrument, and random variance components for five parameters are shown in Figure 2, determined from a single day inter-system study. Subject, visit, and random variance components are shown in Figure 3; determined from a three-day single instrument inter-visit study. All units

are in squared microns (μm^2). Asterisks indicate statistically significant (but very small) contributions of system variance for Temporal, Nasal and Inferior quadrants, as well as clock-hours 9, 1, 3, 4, and 6. There was no significant visit effect for any parameter.

N = 15	Average	Temporal	Superior	Nasal	Inferior
Subject	57.9	116.8	154.2	37.6	224.3
System	-0.04	0.01	-0.2	-0.1	-0.19
Random	2.08	4.26	12.2	5.04	10.46
P-value	0.95	0.33	0.85	1	0.94
Subject	73.1	60.3	174	111.2	228.5
Visit	0.06	0.11*	0.28	0.27*	0.99*
Random	1.7	1.7	9.4	5.4	9.6
P-value	0.1	0.03	0.12	0.05	0

Figure 2

Repeatability, Reproducibility, Coefficient of Variance

Repeatability SD is the square root of the random variance component. Reproducibility is the square root of the sum of all contributors to variance except subject variance. The coefficient of variability (CV) is calculated by dividing the Reproducibility SD by the mean. These results are shown in Figure 3 below; they represent the combined result of both the inter-visit and the inter-instrument study.

	Repeatability SD	Reproducibility SD	Coefficient of Variability
Average	1.33 μm	1.35 μm	1.6%
Temporal	2.03 μm	2.05 μm	3.5%
Superior	3.42 μm	3.45 μm	3.2%
Nasal	2.19 μm	2.24 μm	3.6%
Inferior	3.01 μm	3.14 μm	2.8%
ch9	1.71 μm	1.78 μm	3.7%
ch10	3.53 μm	3.53 μm	5.1%
ch11	4.75 μm	4.77 μm	4.2%
ch12	6.43 μm	6.51 μm	5.9%
ch1	4.84 μm	5.05 μm	4.9%
ch2	4.70 μm	4.74 μm	6.2%
ch3	2.43 μm	2.56 μm	5.0%
ch4	3.25 μm	3.37 μm	5.9%
ch5	4.35 μm	4.37 μm	4.7%
ch6	4.93 μm	5.21 μm	4.3%
ch7	5.00 μm	5.01 μm	4.1%
ch8	3.00 μm	3.00 μm	5.0%

Figure 3

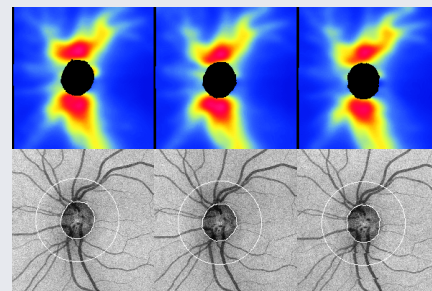
CONCLUSION

The inter-visit variance for Cirrus HD-OCT was not statistically significant for any RNFL thickness parameter. The inter-system variance was not statistically significant for the average RNFL thickness, and it was small for all parameters. The repeatability, reproducibility and coefficient of variability were excellent for all Cirrus HD-OCT RNFL thickness measurements.

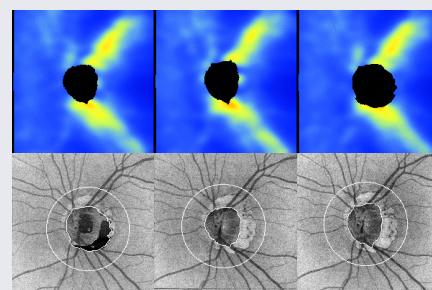
EXAMPLE CASES

Below are RNFL Thickness Maps from a series of scans acquired on a subject during a single visit showing low variance ($<1 \mu\text{m}$ SD) and a different subject showing high variance ($3 \mu\text{m}$ standard deviation in average thickness). The low variance images have reproducible thickness throughout the map, and a reproducibly positioned optic disc. For the high variance subject peripapillary atrophy and poor OCT focus caused the optic disc finding algorithm to fail, so that for at least one scan the calculation circle was not well placed. Using the current software, a user can correct the circle placement, achieving improved reproducibility. Future plans for the Cirrus HD-OCT will allow registration of images prior to progression analysis. This should improve reproducibility for these challenging cases.

Low Variance: $<1 \mu\text{m}$ SD



High Variance: $3 \mu\text{m}$ SD



REFERENCES

1. J. S. Schuman, C.A. Puliafito, and J.G. Fujimoto, *Optical Coherence Tomography of Ocular Diseases*, Second Edition, SLACK Incorporated, Thorofare, NJ, USA, 2004.
2. R. Brancato and B. Lumbroso, *Guide to Optical Coherence Tomography Interpretation*, INC Innovation-News-Communication, Rome, Italy, 2004.
3. A. F. Fercher, C. K. Hitzenberger, W. Drexler, G. Kamp, I. Strasser, H. C. Li, "In vivo Optical Coherence Tomography in Ophthalmology", in *Medical Optical Tomography: Functional Imaging and Monitoring*, G. J. Müller, ed., 355-370, SPIE (1993).
4. D. Koozekanani, C. Roberts, S. E. Katz, and E. E. Herderick, "Intersession Repeatability of Macular Thickness Measurements with the Humphrey 2000 OCT", *Invest. Ophthalmol. Vis. Sci*; 41: 1486 - 1491., May 2000.
5. S. Muscat, S. Parks, E. Kemp and D. Keating, "Repeatability and Reproducibility of Macular Thickness Measurements with the Humphrey OCT System" *Invest. Ophthalmol. Vis. Sci*; 43(2): 490 - 495, February 1, 2002.
6. L. A. Paunescu, J. S. Schuman, L. L. Price, P. C. Stark, S. Beaton, H. Ishikawa, G. Wollstein, and J. G. Fujimoto, "Reproducibility of Nerve Fiber Thickness, Macular Thickness, and Optic Nerve Head Measurements Using StratusOCT", *Invest. Ophthalmol. Vis. Sci.*, 45(6): 1716 – 1724, June 1, 2004.