

Topcon 3D OCT-1 Maestro / 3D OCT-1 Maestro2
REFERENCE DATABASE



Introduction

Optical coherence tomography (OCT) is a noninvasive technique for high-resolution, cross-sectional topographic imaging of tissue by measuring backscattered light.

Glaucoma is a socially critical disease that is a major cause of blindness internationally across many different ethnic groups and ages. According to 2002 WHO statistics, glaucoma is the second leading cause of blindness worldwide¹, and according to a detailed glaucoma epidemiology survey² made in the period of 2000 to 2002, the prevalence of glaucoma for people of 40 years old or above was an estimated 5.0 percent, and in some ethnic populations even higher.³ Optic nerve and field disorders are basically progressive and non-reversible. With glaucoma, the disorder gradually progresses without the subject noticing the disease symptoms. Inhibition or suppression of progress of the disorder by the early detection and early therapy is therefore an important challenge. In the diagnosis of glaucoma, detection of the morphological change in the optic disc or retinal nerve fiber layer thickness is quite important. Findings of the optic disc or retina nerve fiber layer disorder relates to the stage of glaucoma, although such disorder is often detected prior to detection of a visual field loss during an ophthalmology examination. An experienced clinician may effectively observe the fundus oculi of subjects and diagnose glaucoma; however, evaluation of the fundus oculi differs between different clinicians, so that a standardized method for evaluation and decision is desired.

Diabetic retinopathy, a retinal vascular disorder that occurs as a complication of diabetes mellitus (DM), is a leading cause of blindness in the United States, often affecting working-aged adults.⁴ Approximately 4.1 million US adults 40 years and older have diabetic retinopathy; 1 of every 12 persons with DM in this age group has advanced, vision threatening retinopathy.⁵ The Hoorn Study suggests that not only patients with type 2 DM, but elderly individuals with normal glucose metabolism or an impaired glucose metabolism have a substantial risk of developing retinopathy.⁶ Age-related macular degeneration

(AMD) is the leading cause of blindness among European descended people older than 65 years. Age-related macular degeneration affects more than 1.75 million individuals in the United States. Owing to the rapid aging of the US population, this number⁷ will increase to almost 3 million by 2020.⁸

In particular, while age-related macular degeneration has not conventionally found effective therapeutic measures, Visudyne[®] photodynamic therapy and intravitreal drugs such as Lucentis[®] are now available for early detection and treatment options, which in effect will minimize a decline in visual acuity with early diagnoses. It is conceivable that the thickness (or volume) of the retina at the macula can be utilized for early detection of the disorders such as age-related macular degeneration and diabetic retinopathy and follow disease progression and efficacy of the treatment given by the physician.

Topcon provides the 3D OCT-1 Maestro with a Reference Database for the purpose of comparing retinal nerve fiber layer (RNFL), macular thickness ganglion cell layer (GCL) + inner plexiform layer (IPL) and GCL + IPL + RNFL of a subject to a known database of normal individuals, and it serves as a comparison against which measured individual values fall in which under exactly the same scanning pattern. The Reference Database is used to set cut-offs based on the statistical distribution of the eyes in the study. The measured value is considered abnormal or normal according to where the value falls in standard distribution.

- Each subject underwent a complete ophthalmic examination. To be classified as a "Normal Eye" for inclusion in the Reference Database the subject must have met all of the following criteria:
 - a. BSCVA of 20/40 or better
 - b. Intraocular pressure \leq 21 mm Hg bilaterally
 - c. Both eyes must be free of eye disease
 - d. Absence of any of the following conditions or medical history:
 - i. Presence of any ocular pathology except for cataract
 - ii. Narrow angle glaucoma
 - iii. History of leukemia, dementia or multiple sclerosis
 - iv. Concomitant use of hydroxychloroquine and chloroquine
- OCT scans were performed as per the instrument user manual. Image was then automatically segmented and each image was verified as per the user manual for scan acceptability
- The data was collected and statistically analyzed and then submitted to the FDA as part of the 3D OCT-1 Maestro 510K submission for clearance in the United States, K161509.

Institutional Setting

Sites included in the Reference Database were (in alphabetical order):

- Illinois Eye Institute / Illinois College of Optometry
- Jarnagin Primary Eye Care Service / Marshall B. Ketchum University
- New York Veterans Association (VA NY), St Albans Community Living Center
- SUNY College of Optometry
- UAB The University of Alabama, Birmingham
- Valley EyeCare Center
- Western University of Health Sciences

Summary of Database

Enrollment numbers incorporated in this Reference Database are described by scan pattern, age, sex and ethnicity in Table 1, Figure 1 and Figure 2 below.

OCT Scan Patterns

The 12mm x 9mm wide scan pattern and the 6mm x 6mm macula scan pattern were analyzed by 6 sectors, 12 sectors, by 9 sector Early Treatment of Diabetic Retinopathy Study (ETDRS) grid and by the Super Pixel Grid.

The 6mm x 6mm disc scan pattern was analyzed by average RNFL over the TSNIT circle (3.45 mm diameter circle centered on disc), the 4 sectors around the TSNIT circle and by 12 sectors around the TSNIT circle, and by the Super Pixel Grid.

The Super Pixel Grid is made up of the Small and Large Super Pixel Grid. The Small Pixel Grid is made up of 60 x 45 square grids, each 200 microns x 200 microns in size providing 2,700 total grid squares. The Large Pixel Grid is made up of 12x9 square grids, each 1mm x 1mm in size providing 108 total grid squares.

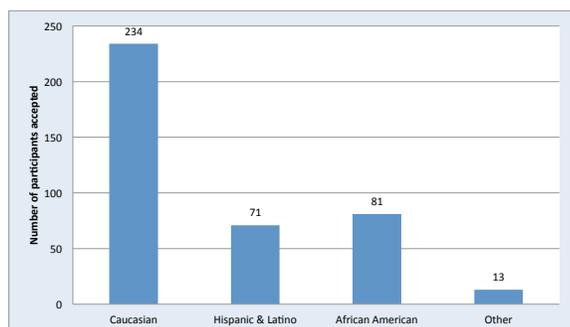


Figure 1. Ethnicity Plot

	Group	n
Age	18-30 years	89
	31-40years	76
	41-50years	66
	51-60years	78
	61-70years	55
	70+ years	35
	Average	46.3
	SD	16.3
	Min	18
Gender	Female	226
	Male	173

Table 1. Enrollment by Age Group and Gender

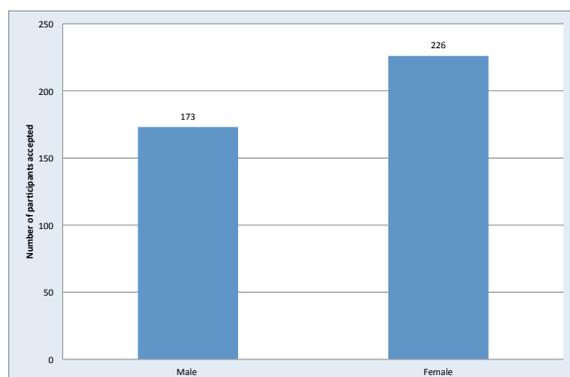


Figure 2. Age Plot

	12mm x 9mm 3D wide	6mm x 6mm 3D macula	6mm x 6mm 3D Disc
Full Retinal Thickness	○	○	
Ganglion cell + IPL Thickness	○	○	
GCL + IPL + RNFL Thickness	○	○	
RNFL Thickness	○		○
TSNIT Circle profile	○		○
Optic Disc	○		○
Super pixel grid	○	○	○

Table 2. Scan Patterns

RNFL Thickness

Median, Mean and Standard Deviation (4 Sector)

Table 3 presents the descriptive statistics of the retinal nerve fiber layer (RNFL) thickness of the full analysis population (Figure 3a). Figures 3b and 3c display the regression lines for the 1st, 5th, 95th and 99th percentile reference limits by age for the RNFL thickness (quadrant) at the average disc area from the Maestro 12x9 3D Wide and the 6x6 3D Disc, respectively.

Scan Pattern		T	S	N	I	Total
12mm x 9mm	N	398	398	398	398	398
	Median	76.13	128.9	79.41	134.8	105.225
	Mean	76.639	125.5	80.569	136.27	104.72
	SD	12.179	18.61	16.333	17.415	11.829
	CI 95%	75.439 77.84	123.7 127.3	78.96 82.179	134.85 138.28	103.555 105.886
6mm x 6mm	N	398	398	398	398	398
	Median	73.435	126.3	78.345	134.8	103.99
	Mean	73.528	126.7	79.499	136.56	104.036
	SD	11.812	17.77	16.461	17.415	11.341
	CI 95%	72.364 74.692	124.9 128.4	77.877 81.121	134.82 138.28	102.918 105.153

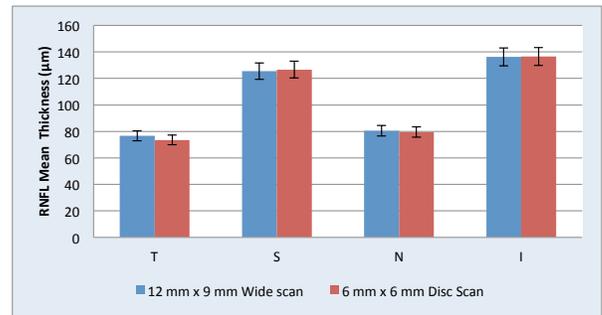
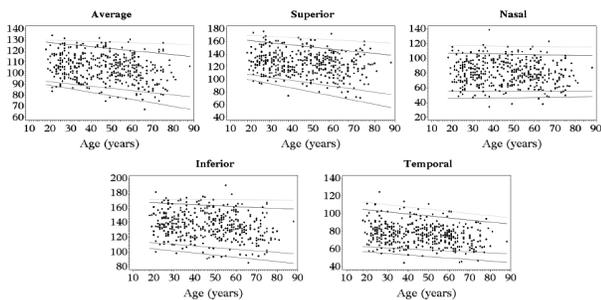


Figure 3a. RNFL Thickness

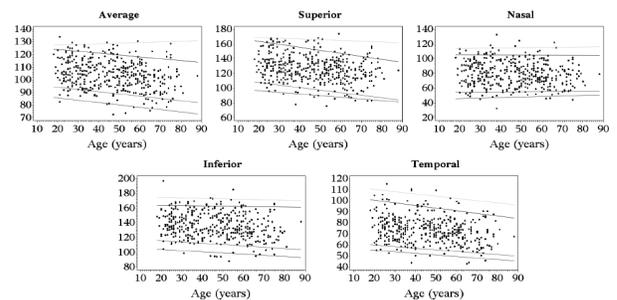
Table 3. RNFL Thickness-Mean (mm)



Red: 1st percentile; Green: 5th percentile; Blue: 95th percentile; Cyan: 99th percentile Program: Topcon\Maestro\3D\BCE\prod\program\BCE_reflimits_cor_nfl_4mm (17OCT2015 17:53:30)

RNFL THICKNESS (QUADRANTS) AT AVERAGE DISC AREA BY AGE - MAESTRO (12X9 3D WIDE) - REFERENCE LIMITS

Figure 3b.



Red: 1st percentile; Green: 5th percentile; Blue: 95th percentile; Cyan: 99th percentile Program: Topcon\Maestro\3D\BCE\prod\program\BCE_reflimits_cor_nfl_4mm (17OCT2015 17:53:30)

RNFL THICKNESS (QUADRANTS) AT AVERAGE DISC AREA BY AGE - MAESTRO (6X6 DISC) - REFERENCE LIMITS

Figure 3c.

Peripapillary RNFL Thickness Median, Mean and Standard Deviation (12 Sector)

Table 4 presents the descriptive statistics of the retinal nerve fiber layer (RNFL) thickness of the full analysis population (Figure 4a).

Figures 4b and 4c display the regression lines for the 1st, 5th, 95th and 99th percentile reference limits by age for the RNFL thickness (clock hour) at the average disc area from the Maestro 12x9 3D Wide and the 6x6 3D Disc, respectively.

Scan Pattern		T	TS	ST	S	SN	NS	N	NI	IN	I	IT	TI	
12mm x 9mm	N	398	398	398	398	398	398	398	398	398	398	398	398	
	Median	63.745	90.53	136.945	122.6	117.575	94.88	65.79	77.78	114.795	150.15	141.18	72.505	
	Mean	64.291	91.514	136.128	123.754	116.576	95.981	66.712	78.999	116.127	151.229	141.11	74.127	
	SD	9.356	17.142	23.813	28.027	24.568	22.084	13.799	19.237	25.824	28.446	23.613	15.135	
	CI 95%		63.369	89.825	133.782	120.993	114.155	93.804	65.353	77.103	113.582	148.425	138.783	72.635
			65.213	93.203	138.475	126.516	118.997	98.157	68.072	80.895	118.672	154.032	143.437	75.618
6mm x 6mm	N	398	398	398	398	398	398	398	398	398	398	398	398	
	Median	60.6	86.965	137.72	125.955	117.905	95.67	63.67	75.35	114.62	150.035	141.455	69.62	
	Mean	61.309	87.965	136.062	126.323	117.526	96.561	64.953	76.993	116.055	151.966	141.277	71.313	
	SD	9.142	16.359	24.304	27.583	23.88	22.255	13.785	19.399	25.303	27.748	24.428	14.74	
	CI 95%		60.408	86.353	133.667	123.605	115.172	94.368	63.595	75.082	113.562	149.231	138.87	69.86
			62.21	89.577	138.457	120.041	119.879	98.754	66.311	78.905	118.549	154.7	143.685	72.766

Table 4. RNFL Thickness

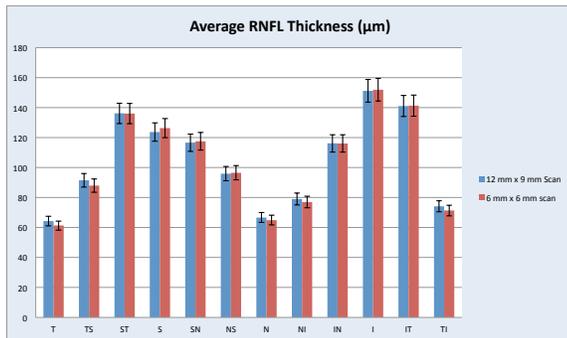
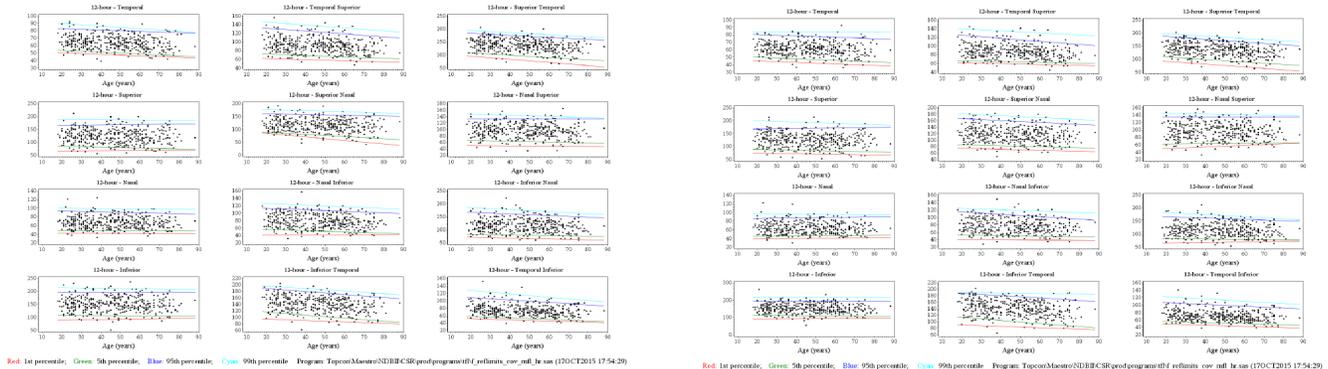


Figure 4a.



RNFL THICKNESS (CLOCK HOUR) AT AVERAGE DISC AREA BY AGE - MAESTRO (12X9 3D WIDE) - REFERENCE LIMITS

RNFL THICKNESS (CLOCK HOUR) AT AVERAGE DISC AREA BY AGE - MAESTRO (6X6 DISC) - REFERENCE LIMITS

Macular 3D Retinal Median, Mean and Standard Deviation (ETDRS)

Table 5 presents the descriptive statistics of the full retinal thickness in the full analysis population. 395 of the 399 subjects in the full analysis population had scans available for measurements. Four patients were excluded from this analysis, as all of their scans

were determined to be unacceptable by the Reading Center.

Figures 5b and 5c display the regression lines for the 1st, 5th, 95th and 99th percentile reference limits by age for the full retinal thickness from the Maestro 12x9 3D Wide and the 6x6 3D Disc, respectively.

Scan Pattern		Center Fovea	Superior Parafoveal	Nasal Parafoveal	Inferior Parafoveal	Temporal Parafoveal	Superior Perifoveal	Nasal Perifoveal	Inferior Perifoveal	Temporal Perifoveal
12mm x 9mm	N	395	395	395	395	395	395	395	395	395
	Median	235.52	308.28	309.56	306.92	297.74	270.05	284.75	257.86	255.8
	Mean	237.079	308.138	309.494	306.13	297.548	269.009	284.588	257.721	255.347
	SD	20.889	15.96	16.311	15.985	15.296	14.968	16.447	14.601	13.906
	CI 95%	235.012 239.146	306.56 309.717	307.88 311.107	304.549 307.712	296.035 299.061	267.528 270.489	282.961 286.215	256.276 259.165	253.971 256.722
6mm x 6mm	N	395	395	395	395	395	395	395	395	395
	Median	232.29	308.98	309.08	305.78	296.75	269.75	284.21	258.07	253.4
	Mean	234	308.985	309.335	305.732	296.593	269.505	284.153	258.579	252.926
	SD	20.657	16.192	16.685	16.322	16.625	15.165	16.423	14.909	13.94
	CI 95%	231.956 236.043	307.383 310.587	307.685 310.986	304.117 307.346	295.047 298.139	268.005 271.006	282.529 285.778	257.105 260.054	251.547 254.305

Table 5. Full Retinal Thickness

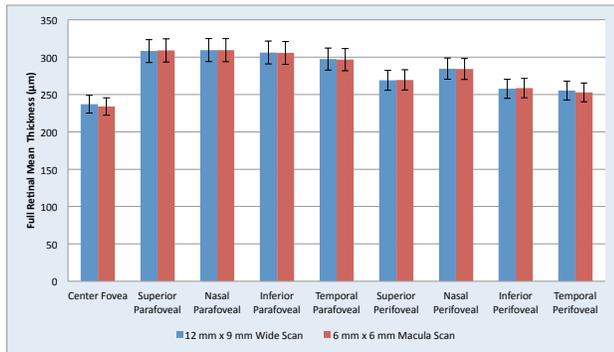


Figure 5a. Full Retinal Thickness

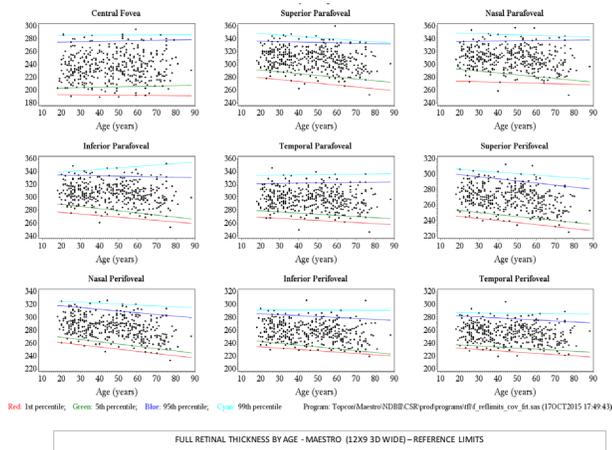


Figure 5b.

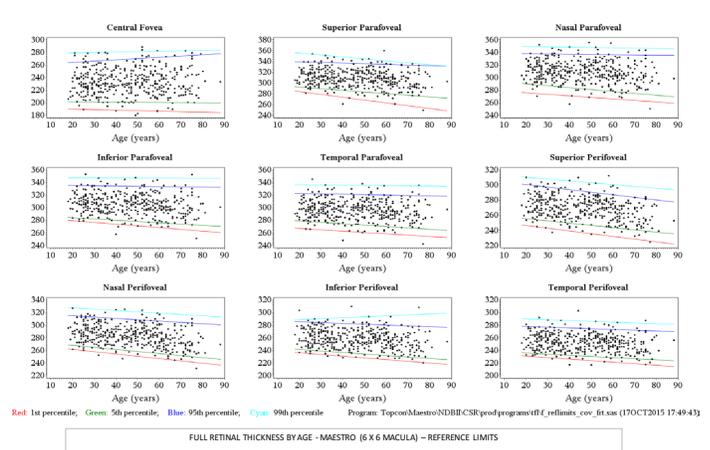


Figure 5c.

Ganglion Cell Analysis

Reference data for the study population was collected for the following parameters associated with the ganglion cell thickness (see Figure 6a):

1. Superior thickness (1-6mm diameter circle)
2. Superior nasal thickness (1-6mm diameter circle)
3. Superior temporal thickness (1-6mm diameter circle)
4. Inferior thickness (1-6mm diameter circle)
5. Inferior nasal thickness (1-6mm diameter circle)
6. Inferior temporal thickness (1-6mm diameter circle)
7. Average thickness (1-6mm diameter circle)

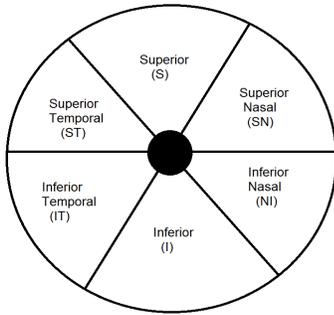


Figure 6a. GCL-Macula 6 Sector Grid

Scan Pattern	S	SN	ST	I	IN	IT	AVER	
12mm x 9mm	N	398	398	398	398	398	398	
	Median	70.305	74.73	71.3	66.975	73.305	72.135	71.45
	Mean	70.063	74.469	70.991	67.305	72.994	73.322	71.363
	SD	6.149	6.566	6.296	5.863	6.459	6.192	5.924
	CI 95%	69.457	73.822	70.371	66.728	72.357	71.712	70.779
		70.669	75.116	71.612	67.883	73.63	72.932	71.946
6mm x 6mm	N	397	397	397	397	397	397	
	Median	70.42	74.8	71.68	67.81	73.36	72.28	71.7
	Mean	70.394	74.521	71.475	68.19	73.124	72.525	71.726
	SD	6.224	6.506	5.924	6.139	6.515	6.01	5.88
	CI 95%	69.78	73.879	70.891	67.585	73.481	71.932	71.146
		71.008	75.163	72.06	68.796	73.767	73.118	72.306

Table 6.

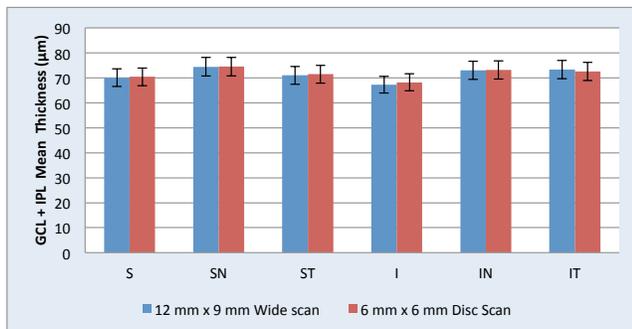


Figure 6. GCL + IPL Thickness Mean (mm)

Table 6 presents the descriptive statistics of the ganglion cell + IPL thickness of the full analysis population (Figure 6).

Table 7 presents the descriptive statistics of the ganglion cell complex thickness of the full analysis population (Figure 7a).

Scan Pattern	S	SN	ST	I	IN	IT	AVER	
12mm x 9mm	N	398	398	398	398	398	398	
	Median	105.705	116.55	94.08	104.465	116.98	97	105.85
	Mean	105.74	116.728	93.828	104.669	117.43	96.708	105.949
	SD	8.944	10.002	7.298	8.791	10.999	96.708	8.533
	CI 95%	104.858	115.742	93.109	103.802	116.346	95.991	105.108
		106.621	117.714	94.547	105.535	118.514	97.424	106.789
6mm x 6mm	N	397	397	397	397	397	397	
	Median	106.72	117.15	93.43	105.67	117.49	96.29	105.8
	Mean	106.698	116.85	93.331	105.702	117.971	96.254	106.268
	SD	9.094	9.915	7.314	9.079	10.966	7.361	8.602
	CI 95%	105.801	115.871	92.609	104.806	116.889	95.528	105.419
		107.595	117.828	94.052	106.597	119.053	96.981	107.116

Table 7.

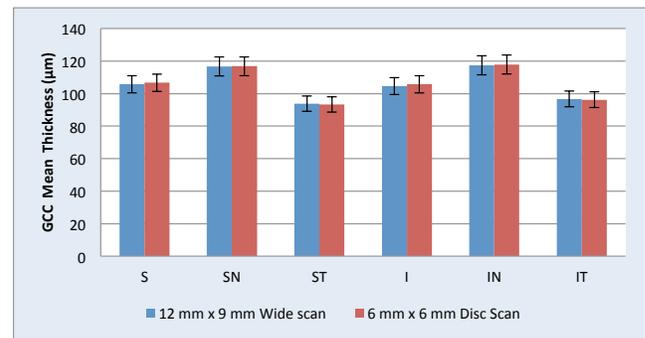
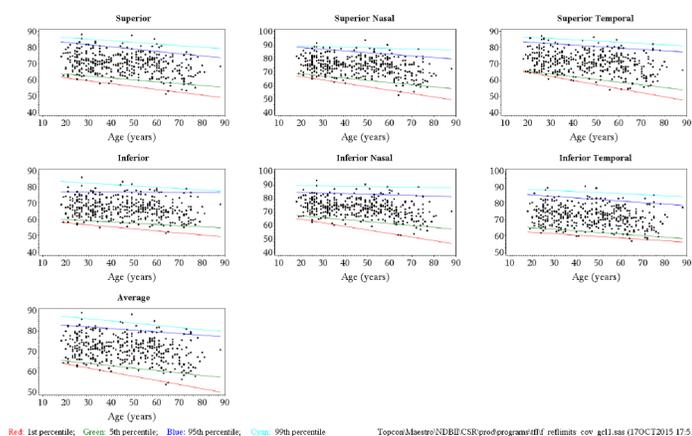


Figure 7a.

Ganglion Cell Analysis

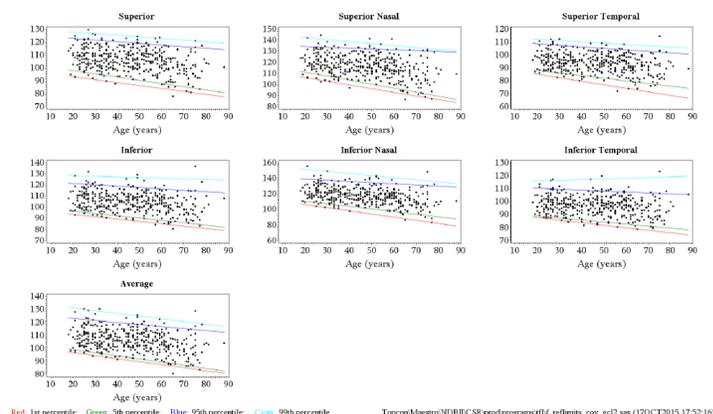
Figures 6b and 6c display the regression lines for the 1st, 5th, 95th and 99th percentile reference limits by age for ganglion cell + IPL thickness from the Maestro 12x9 3D Wide and the 6x6 3D Macula, respectively.

Figures 7b and 7c display the regression lines for the 1st, 5th, 95th and 99th percentile reference limits by age for the ganglion cell complex thickness from the Maestro 12x9 3D Wide and the 6x6 3D Macula, respectively.



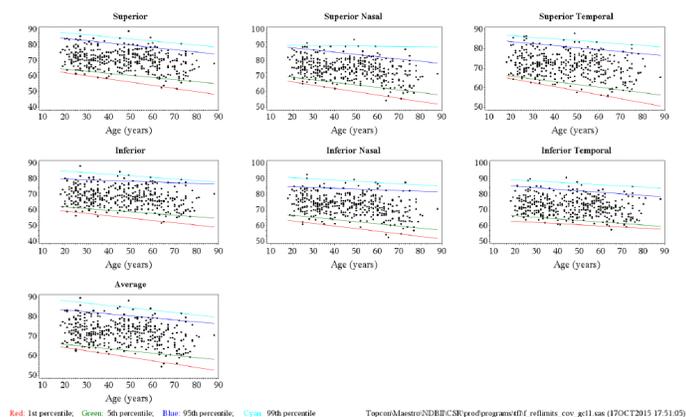
GANGLION CELL + IPL THICKNESS BY AGE - MAESTRO (12X9 3D WIDE) - REFERENCE LIMITS

Figure 6b.



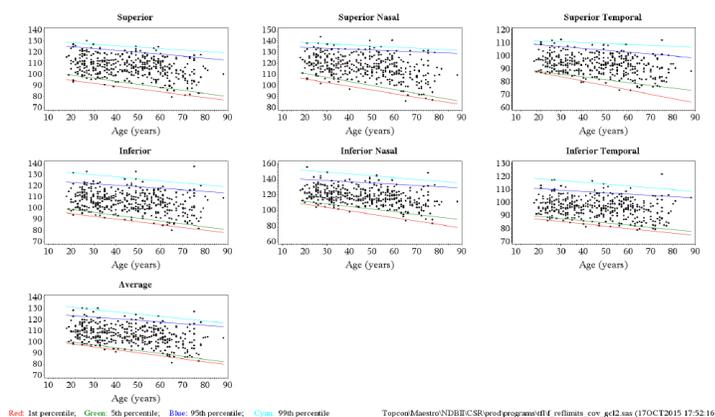
GCL + IPL + RNFL Thickness By Age - Maestro (12x9 3D Wide) - Reference Limits

Figure 7b.



GANGLION CELL + IPL THICKNESS BY AGE - MAESTRO (6X6 MACULA) - REFERENCE LIMITS

Figure 6c.



GCL + IPL + RNFL Thickness By Age - Maestro (6x6 MACULA) - Reference Limits

Figure 7c.

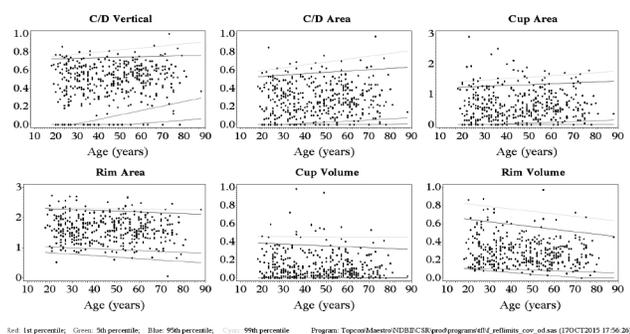
Disc Segmentation Analysis

Table 8 presents the descriptive statistics of the optic disc of the full analysis population.

Figures 8a and 8b display the regression lines for the 1st, 5th, 95th and 99th percentile reference limits of the optic disc at average disc area by age from the Maestro 12x9 3D Wide and the 6x6 3D Disc, respectively.

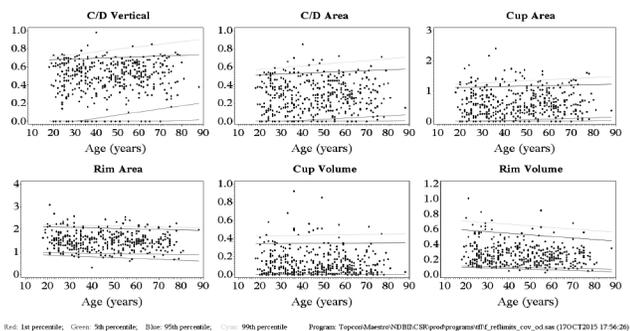
Scan Pattern		C/D	C/D	Disc	Cup	Rim	Cup Vol	Rim Vol
12mm x 9mm	N	398	398	398	398	398	398	398
	Median	0.52	0.26	2.23	0.57	1.58	0.08	0.26
	Mean	0.489	0.278	2.264	0.655	1.608	0.127	0.287
	SD	0.2	0.179	0.409	0.485	0.415	0.143	0.153
	CI 95%	0.469 0.508	0.261 0.296	2.223 2.304	0.608 0.703	1.568 1.649	0.112 0.141	0.272 0.302
6mm x 6mm	N	398	398	398	398	398	398	398
	Median	0.51	0.27	2.065	0.545	1.46	0.08	0.24
	Mean	0.48	0.28	2.102	0.613	1.489	0.125	0.264
	SD	0.19	0.169	0.414	0.432	0.383	0.135	0.14
	CI 95%	0.462 0.499	0.263 0.297	2.061 2.142	0.57 0.655	1.452 1.527	0.112 0.139	0.25 0.278

Table 8



Optic Disc At Average Disc Area By Age - Maestro (12x9 3D Wide) - Reference Limits

Figure 8a.



Optic Disc At Average Disc Area By Age - Maestro (6x6 DISC) - Reference Limits

Figure 8b.

Summary

Topcon has incorporated a Reference Database into the Topcon 3D OCT-1 Maestro instrument. This age stratified Reference Database is comprised of several ethnicities all collected in the United States. These data were submitted to the FDA as per the 3D OCT-1 Maestro 510K submission.

References

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