7 Reference Database

7.1 BMO-MRW Reference Database

Composition

The BMO-MRW reference database includes 246 eyes (123 right eyes and 123 left eyes) of 246 normal subjects (109 male and 137 female) of European descent with mean age of 52.2 years (range 20 to 87 years). Subjects were enrolled in a prospective, multi-center, observational study. Included subjects had healthy eyes without prior intraocular surgery (except cataract surgery or Lasik) and without clinically significant vitreal, retinal or choroidal diseases, diabetic retinopathy, or disease of the optic nerve, no history of glaucoma, intraocular pressure ≤21 mmHg, best corrected visual acuity ≥0.5, refraction between +6 and -6 diopters, astigmatism ≤2 diopters, normal visual field with Glaucoma Hemifield Test and Mean Deviation within normal limits, clinically normal appearance of optic disc with normal appearing neuroretinal rim with respect to color and shape.

BMO-MRW reference data was acquired and analyzed relative to the fovea-to-BMO-center axis, to ensure accurate and consistent positioning of the BMO-MRW profiles across eyes.

The age- and BMO area-adjusted BMO-MRW normal distribution percentiles were computed. The distribution percentiles are used to determine whether an examined eye has measures within or outside the normal range.

The reference database is limited by its sample size (246 eyes of 246 subjects), the covered age range (20 to 87 years), the covered range of optic disc size (BMO area 1.0 to 3.4 mm^2; 8 cases with BMO area >2.5 mm^2), the covered range of refraction (+6 to -6 diopters), and European ethnicity.

> ⚠️ **CAUTION!**
> Consider the reference database limitations described above when examining subjects whose characteristics differ from those included in the reference database.

Adjustment for age and for BMO area

BMO-MRW decreases with increasing age and with increasing BMO area. To take this into account, the reference database is adjusted for age and BMO area in a multiple linear regression model. As a result, the percentiles of the normal distribution used for the classification depend on the patient's age and the eye's BMO area.

The BMO-MRW value r_i that corresponds to a certain normal distribution percentile i for a subject of given age and BMO area, and the normal distribution percentile p_r that corresponds to a measured value of BMO-MRW for a subject of given age and BMO area, are computed as follows:

The ith age- and BMO area-adjusted percentile of BMO-MRW r_i for a subject with age a and BMO area b is given by
$$r_i = \bar{r} + \sigma_r F^{-1}(i/100) + s_{ra}(a - \bar{a}) + s_{rb}(b - \bar{b}).$$

The age- and BMO area-adjusted percentile p_r corresponding to a measured BMO-MRW r for a subject with age a and BMO area b is given by $p_r = F(Z)$, $Z = (r - s_{ra}(a - \bar{a}) - s_{rb}(b - \bar{b}) - \bar{r})/\sigma_r$

- $\bar{r}$ = mean BMO-MRW in the reference database (age- and BMO area-adjusted)
- σ_r = standard deviation of BMO-MRW in the reference database (age- and BMO area-adjusted)
- $\bar{a}$ = mean age of the subjects in the reference database
- $\bar{b}$ = mean BMO area of the eyes in the reference database
- s_{ra} = slope of the regression of BMO-MRW versus age
- s_{rb} = slope of the regression of BMO-MRW versus BMO area
- $F(Z)$ = cumulative distribution function of the normal distribution
- $F^{-1}(p)$ = inverse of the cumulative distribution function of the normal distribution

Mean age and mean BMO area in the reference database are as follows:

- Mean age $\bar{a}$ = 52.17 years
- Mean BMO area $\bar{b}$ = 1.781 mm^2

The means $\bar{r}$, standard deviations σ_r, and slopes s_{ra} and s_{rb} for BMO-MRW global and in the six standard sectors temporal (T), temporal-superior (TS), temporal-inferior (TI), nasal (N), nasal-superior (NS), and nasal-inferior (NI) are listed in the following table:

	$\bar{r}$ [µm]	σ_r [µm]	s_{ra} [µm/year]	s_{rb} [µm/mm^2]
BMO-MRW Global	336.1	51.63	-1.3390	-48.795
BMO-MRW T	238.7	42.83	-1.0286	-35.353
BMO-MRW TS	321.1	59.87	-1.4527	-40.840
BMO-MRW TI	352.4	60.25	-1.5594	-23.402
BMO-MRW N	374.2	63.67	-1.2828	-72.949
BMO-MRW NS	374.2	71.09	-1.4747	-48.672
BMO-MRW NI	411.6	71.87	-1.7216	-46.052

As an example for the effect of age and BMO area, the following tables show the values of the 1st and the 5th percentiles of BMO-MRW for the global average and the averages in the standard sectors, for a 45 years old subject with a small BMO area (1.5 mm^2), and for a 65 years old subject with a large BMO (2.5 mm^2).

BMO-MRW, age 45 years, BMO area 1.5 mm^2

	1st percentile [µm]	5th percentile [µm]
Global	239	275
Temporal	156	186
Temporal-superior	204	245
Temporal-inferior	230	271
Nasal	256	299
Nasal-superior	233	282
Nasal-inferior	270	319

BMO-MRW, age 65 years, BMO area 2.5 mm^2

	1st percentile [µm]	5th percentile [µm]
Global	164	199
Temporal	100	130
Temporal-superior	134	175
Temporal-inferior	175	217
Nasal	157	201
Nasal-superior	155	203
Nasal-inferior	189	238

7.2   RNFL Thickness Reference Database

Composition   The RNFLT reference database includes 218 eyes (111 right eyes and 107 left eyes) of 218 normal subjects (94 male and 124 female) of European descent with mean age of 51.5 years (range 20 to 87 years). Subjects were enrolled in a prospective, multi-center, observational study. Included subjects had healthy eyes without prior intraocular surgery (except cataract surgery or Lasik) and without clinically significant vitreal, retinal or choroidal diseases, diabetic retinopathy, or disease of the optic nerve, no history of glaucoma, intraocular pressure ≤21 mmHg, best corrected visual acuity ≥0.5, refraction between +6 and -6 diopters, astigmatism ≤2 diopters, normal visual field with Glaucoma Hemifield Test and Mean Deviation within normal limits, clinically normal appearance of optic disc with normal appearing neuroretinal rim with respect to color and shape.

RNFLT reference data was acquired and analyzed relative to the fovea-to-BMO-center axis, to ensure accurate and consistent positioning of the BMO-MRW profiles across eyes. The age- and BMO area-adjusted RNFLT normal distribution percentiles were computed. The distribution percentiles are used to determine whether an examined eye has measures within or outside the normal range.

The RNFLT reference database includes reference data for RNFL thickness along peri-papillary circle scans with 3.5 mm, 4.1 mm, and 4.7 mm diameter.

RNFL Thickness Reference Database

The reference database is limited by its sample size (218 eyes of 218 subjects), the covered age range (20 to 87 years), the covered range of optic disc size (BMO area 1.0 to 3.4 mm^2; 8 cases with BMO area >2.5 mm^2), the covered range of refraction (+6 to -6 diopters), and European ethnicity.

⚠️ **CAUTION!**
Consider the reference database limitations described above when examining subjects whose characteristics differ from those included in the reference database.

Adjustment for age and for BMO area

RNFL thickness in normal subjects decreases slightly with increasing age and with decreasing BMO area. To take this into account the reference database is age-adjusted and BMO area-adjusted based on multiple linear regression. As a result, the percentiles of the normal distribution used for the classification depend on the patient's age and the eye's BMO area.

The RNFLT value r_i that corresponds to a certain normal distribution percentile i for a subject of given age and BMO area, and the normal distribution percentile p_r that corresponds to a measured value of RNFLT for a subject of given age and BMO area, are computed as follows:

The ith age- and BMO area-adjusted percentile of RNFLT r_i is given by $r_i = \bar{r} + \sigma_r F^{-1}(i/100) + s_{ra}(a - \bar{a}) + s_{rb}(b - \bar{b})$.

The age- and BMO area-adjusted percentile p_r corresponding to a measured RNFLT r for a subject with age a and BMO area b is given by $p_r = F(Z)$, $Z = (r - s_{ra}(a - \bar{a}) - s_{rb}(b - \bar{b}) - \bar{r})/\sigma_r$.

- $\bar{r}$ = mean RNFLT in the reference database (age- and BMO area-adjusted)
- σ_r = standard deviation of the RNFLT in the reference database (age- and BMO area-adjusted)
- $\bar{a}$ = mean age of the subjects in the reference database
- $\bar{b}$ = mean BMO area of the eyes in the reference database
- s_{ra} = slope of the regression of RNFLT versus age
- s_{rb} = slope of the regression of RNFLT versus BMO area
- $F(Z)$ = cumulative distribution function of the normal distribution
- $F^{-1}(p)$ = inverse of the cumulative distribution function of the normal distribution

Mean age and mean BMO area in the reference database are as follows:

- Mean age $\bar{a}$ = 51.51 years
- Mean BMO area $\bar{b}$ = 1.773 mm^2

The means $\bar{r}$, standard deviations σ_r, and slopes s_{ra} and s_{rb} for RNFLT global and in the six standard sectors temporal (T), temporal-superior (TS), temporal-inferior (TI), nasal (N), nasal-superior (NS), and nasal-inferior (NI) are listed in the following tables for circle diameters 3.5 mm, 4.1 mm and 4.7 mm:

RNFLT (3.5 mm circle diameter)

	$\bar{r}$ [µm]	σ_r [µm]	s_{ra} [µm/year]	s_{rb} [µm/mm^2]
RNFLT Global	97.8	8.6	-0.1872	6.390
RNFLT T	70.5	9.8	-0.0502	2.338
RNFLT TS	128.0	19.6	-0.1591	11.333
RNFLT TI	148.8	16.9	-0.3357	11.783
RNFLT N	81.5	12.5	-0.1558	4.035
RNFLT NS	112.0	22.4	-0.2718	10.239
RNFLT NI	109.5	21.5	-0.3820	7.919

RNFLT (4.1 mm circle diameter)

	$\bar{r}$ [µm]	σ_r [µm]	s_{ra} [µm/year]	s_{rb} [µm/mm^2]
RNFLT Global	84.2	7.4	-0.1474	5.529
RNFLT T	63.3	8.8	-0.0471	3.024
RNFLT TS	117.7	16.6	-0.1091	11.727
RNFLT TI	133.4	15.0	-0.3096	9.949
RNFLT N	68.0	10.1	-0.1057	3.385
RNFLT NS	90.2	18.7	-0.2090	6.705
RNFLT NI	87.4	17.8	-0.3045	5.366

RNFLT (4.7 mm circle diameter)

	$\bar{r}$ [µm]	σ_r [µm]	s_{ra} [µm/year]	s_{rb} [µm/mm^2]
RNFLT Global	73.9	6.6	-0.1188	4.385
RNFLT T	58.3	7.8	-0.0368	2.801
RNFLT TS	107.8	14.6	-0.0900	10.116
RNFLT TI	119.8	14.0	-0.2937	7.768
RNFLT N	58.6	8.5	-0.0667	2.497
RNFLT NS	74.4	15.2	-0.1860	3.659
RNFLT NI	71.2	14.4	-0.2327	4.826

As an example for the effect of age and BMO area, the following tables show the values of the 1st and the 5th percentiles of the average RNFLT (3.5mm diameter circle) global and in the standard sectors, for a 45 years old subject with a large BMO area (2.5 mm^2), and for a 65 years old subject with a small BMO area (1.5 mm^2).

RNFL Thickness Reference Database

RNFLT (3.5 mm circle diameter), age 45 years, BMO area 2.5 mm^2

	1st percentile [µm]	5th percentile [µm]
Global	83.6	89.5
Temporal	49.7	56.4
Temporal-superior	91.7	105.1
Temporal-inferior	120.0	131.7
Nasal	56.3	64.8
Nasal-superior	69.1	84.4
Nasal-inferior	67.8	82.4

RNFLT (3.5 mm diameter circle), age 65 years, BMO area 1.5 mm^2

	1st percentile [µm]	5th percentile [µm]
Global	73.5	79.4
Temporal	46.4	53.1
Temporal-superior	77.2	90.5
Temporal-inferior	101.7	113.2
Nasal	49.2	57.7
Nasal-superior	53.4	68.7
Nasal-inferior	52.5	66.8