DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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May 6, 2016

Heidelberg Engineering Gmbh
% Ms. Diane Horwitz
Mandell Horwitz Consultants LLC
2995 Steven Martin Drive
Fairfax, Virginia 22031

Re: K152205
Trade/Device Name: Spectralis Hra + Oct And Variants (e.g.s Below), Spectralis Fa+oct, Spectralis Icga+oct, Spectralis Oct Blue Peak, Spectralis Oct Ith Multicolor
Regulation Number: 21 CFR 886.1570
Regulation Name: Ophthalmoscope
Regulatory Class: Class II
Product Code: OBO, MYC,
Dated: March 29, 2016
Received: March 30, 2016

Dear Ms. Horwitz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing

(21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kesia Alexander

for Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic and Ear,
Nose and Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
*See PRA Statement below.*

510(k) Number *(if known)*

Device Name
Spectralis HRA+OCT with RNFL and ONH Normative Database

Indications for Use *(Describe)*

The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for viewing the posterior segment of the eye, including two- and three-dimensional imaging, cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT), fundus photography, fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA), autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT BluePeak) and to perform measurements of ocular anatomy and ocular lesions. The device is indicated as an aid in the detection and management of various ocular diseases, including age-related macular degeneration, macular edema, diabetic retinopathy, retinal and choroidal vascular diseases, glaucoma, and for viewing geographic atrophy as well as changes in the eye that result from neurodegenerative diseases. The SPECTRALIS HRA+OCT and SPECTRALIS OCT include normative databases for retinal nerve fiber layer thickness and optic nerve head neuroretinal parameter measurements, which are used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values found in normal subjects.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.**

**FOR FDA USE ONLY**

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

# 510(k) Summary

## I. Submitter

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Contact Person: Dr. Christian Elm
Date Summary Prepared: May 4, 2016

## II. Device

Trade/Device Name: SPECTRALIS HRA+OCT and Variants
Common/Usual Name: Retina Angiograph / Optical Coherence Tomograph
Classification Name: Tomography, Optical Coherence (21 CFR 886.1570)
Regulatory Class: II
Product Code: OBO, MYC

## III. Predicate Device

Heidelberg SPECTRALIS HRA+OCT, K101223, amended by K121993
Reference devices include other medical devices

- with wide field objective: Nidek Ophthalmoscope F-10, K072259
- with ultra-widefield objective: Optos 200 T, K111628

## IV. Device Description

The SPECTRALIS HRA+OCT is a real-time imaging system of anterior and posterior segments of the human eye and for aiding in the assessment and management of various diseases of the posterior segment, such as age-related macular degeneration, diabetic retinopathy, and glaucoma.

The device is a combination of optical coherence tomography (OCT) with confocal scanning laser ophthalmoscopy (cSLO). OCT imaging includes high-resolution cross-sectional imaging of ocular structures (e.g., retina, macula, optic nerve head); cSLO imaging includes high-resolution and dynamic infrared reflectance, blue reflectance, fluorescein angiography, indocyanine green angiography, and autofluorescence imaging. OCT images and cSLO images are acquired simultaneously and are viewed side-by-side on the computer screen. Images are acquired and stored using SPECTRALIS operation software, which runs on a standard personal computer. SPECTRALIS components include a laser scanning camera, camera mount with headrest, operation panel, power supply box, operation software, and host computer. A MultiColor option is included to provide additional green reflectance imaging and a “composite color” image, which provides a different view of the features of the eye. This composite color image is not the same as fundus color photo. This submission includes Enhanced Depth Imaging (EDI) as an optional viewing mode that allows for better visualization of deep eye structures below the retina.

## V. Intended Use/Indications for Use

The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for viewing the posterior segment of the eye, including two- and three-dimensional imaging, cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT), fundus photography,

fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA), autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT with BluePeak) and to perform measurements of ocular anatomy and ocular lesions. The device is indicated as an aid in the detection and management of various ocular diseases, including age-related macular degeneration, macular edema, diabetic retinopathy, retinal and choroidal vascular diseases, glaucoma, and for viewing geographic atrophy as well as changes in the eye that result from neurodegenerative diseases. The SPECTRALIS HRA+OCT and SPECTRALIS OCT include reference databases for retinal nerve fiber layer thickness and optic nerve head neuroretinal rim parameter measurements, which are used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values found in normal subjects.

## VI. Comparison of Technological Characteristics with the Predicate Device

The basic technological characteristics of the SPECTRALIS predicate, with software version 5.6, and the new device, with software version 6.0, remain the same. The new device has been updated in the following ways:

- The new device includes a new reference database that includes optic nerve head (ONH) neuroretinal rim width measurements for the parameter BMO-MRW in addition to retinal nerve fiber layer (RNFL) thickness.
- The method for locating the fovea and the optic disc center (FoDi) were modified to result in a more accurate definition of both locations with the revised imaging software. The FoDi method is based on an IR image of the fundus, the new, more accurate definition is called Anatomic Positioning System (APS) and is based on OCT images of the fundus. It uses the fovea and the BMO center as landmarks and aligns the image axis on the fovea-BMO center axis.
- A new scan pattern called ONH-RC, which includes RNFL thickness measurements with three fixed diameter circles of 3.5, 4.1 and 4.7 mm diameter and 48 radial scans around the BMO center. The ONH-RC scan pattern measures the parameter BMO-MRW (BMO minimum rim width) with an image orientation based on APS information
- An additional imaging function, Enhanced Depth Imaging (EDI), is added to enhance viewing the deep structures of the eye. EDI is available for standard OCT preset scan pattern only. It allows for standard segmentation of ILM and RNFL and retinal thickness measurement. Reference data are not available for EDI scans.
- Two optional accessory lenses have been added to allow the user conveniently to view a greater proportion of the posterior eye in one view: the Wide Field Objective and the Ultra-Widefield Objective. Both objectives are used for SLO imaging only.

The differences between the predicate device and the subject device are shown in **Table 1**.

**TABLE 1: COMPARISON OF CHANGED PRIMARILY CHARACTERISTICS**

| | **Predicate Device (SPECTRALIS HRA+OCT) K101223 and amended in K121993** | **Subject Device** |
|---|---|---|
| Optical image axis | Manually determined, FoDi based, using IR images, horizontally aligned | Semi-automatic aligned, APS based, using OCT images, aligned along the fovea-BMO center axis |

**TABLE 1: COMPARISON OF CHANGED PRIMARILY CHARACTERISTICS**

| | Predicate Device (SPECTRALIS HRA+OCT) K101223 and amended in K121993 | Subject Device |
|---|---|---|
| Measurement of RNFLT | Using 12° fixed degree circle scan pattern | Using 3.5mm, 4.1mm and 4.7 mm fixed diameter circle scan pattern |
| Measurement of ONH neuroretinal rim width | Using 24 | Using 48 BMO-centered radial scans |
| Reference database for ONH neuroretinal rim with and RNFLT | Caucasian population, RNFLT only | Population of different races and ethnicities from Canada, Germany, and US, representing the population mix of the U.S.A. RNFLT and BMO-MRW |
| EDI imaging | No | Yes |
| Scan angle options | 30° (standard lens) | 30° (standard lens), 55° (WFO) and 102° (UWF) |

These differences were verified with clinical and bench testing and software verification and validation.

The standard hardware has not been modified compared to the predicate.

## VII. Performance Data

The following performance data were provided in support of the substantial equivalence determination.

**Electrical safety and electromagnetic compatibility (EMC)**
The SPECTRALIS HRA+OCT has been tested according to IEC 60601-1 and IEC 60601-1-2 and was found to meet all requirements.

**Laser Safety**
The system is a laser product of Class 1 according to 21 CFR §1040.10 and complies with IEC 60825-1.

**Software Verification and Validation Testing**
Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a "moderate" level of concern, since a malfunction of or latent design flaw in the software could lead to an erroneous diagnosis or a delay in delivery of appropriate medical care that would lead to minor injury.

A study in normal and glaucomatous human volunteers was conducted to assess precision and agreement of ONH neuroretinal rim parameter and RNFL thickness measurements. The coefficients of variation and the ANOVA analysis for the measured endpoints were within the specified range for this device.

**Clinical Studies**

*RNFL Thickness Reference Database*

The RNFLT reference database includes 330 eyes (167 right eyes and 163 left eyes) of 330 normal subjects (146 male and 184 female) with mean age of 49.7 years (range 20 to 90 years) and of various racial and ethnic origins (non-Hispanic White: 218; Hispanic White: 45; Black or African American: 41; Asian: 23; American Indian / Alaska Native: 3). The racial and ethnic composition of the reference database is representative for the U.S. population. 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 circle scans across eyes.

The first and fifth percentile reference limits for RNFLT were computed and age- and BMO area-adjusted, and used for comparison with the retinal nerve fiber layer thickness from an individual

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.

The reference database is limited by its sample size (330 eyes of 330 subjects), the covered age range (20 to 90 years), the covered range of optic disc size (BMO area 1.0 to 3.4 $mm^2$; 15 cases with BMO area >2.5 $mm^2$), and the covered range of refraction (+6 to -6 diopters).

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.

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

- Mean age = 49.70 years
- Mean BMO area = 1.828 $mm^2$

As an example for the effect of age and BMO area, the following **Table 2** and **Table 3** show the values of the 1st and the 5th percentiles of the average RNFLT (3.5 mm 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 $mm^2$).

**TABLE 2: RNFLT (3.5 MM CIRCLE DIAMETER). AGE 45 YEARS, BMO AREA 2.5 MM$^2$**

| | 1st percentile [µm] | 5th percentile [µm] |
|---|---|---|
| Global | 82.5 | 88.8 |
| Temporal | 48.9 | 55.8 |
| Temporal superior | 86.1 | 100.5 |
| Temporal inferior | 115.3 | 127.5 |
| Nasal | 54.7 | 63.7 |
| Nasal superior | 71.4 | 87.8 |
| Nasal inferior | 66.5 | 82.2 |

**TABLE 3: RNFLT (3.5 MM CIRCLE DIAMETER) AGE 65 YEARS, BMO AREA 1.5 MM$^2$**

| | 1st percentile [µm] | 5th percentile [µm] |
|---|---|---|
| Global | 72.2 | 78.5 |
| Temporal | 45.0 | 51.8 |
| Temporal superior | 72.4 | 86.7 |
| Temporal inferior | 99.6 | 111.8 |
| Nasal | 47.7 | 56.6 |
| Nasal superior | 42.4 | 68.8 |
| Nasal inferior | 51.0 | 66.7 |

*BMO-MRW Reference Database*

The BMO-MRW reference database includes 368 eyes (182 right eyes and 186 left eyes) of 368 normal subjects (165 male and 203 female) with mean age of 50.3 years (range 20 to 90 years) and of various racial and ethnic origins (non-Hispanic White: 246; Hispanic White: 47; Black or African American: 47; Asian: 25; American Indian / Alaska Native: 3). The racial and ethnic composition of the reference database is representative for the U.S. population. Subjects were enrolled in a prospective, multicenter, 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 first and fifth percentile reference limits for BMO-MRW were computed and age- and BMO area-adjusted, and used for comparison with the BMO minimum rim width from an individual

The reference database is limited by its sample size (368 eyes of 368 subjects), the covered age range (20 to 90 years), the covered range of optic disc size (BMO area 1.0 to 3.4 mm$^2$; 19 cases with BMO area >2.5 mm$^2$), and the covered range of refraction (+6 to -6 diopters).

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.

As an example for the effect of age and BMO area, the following **Table 4** and **Table 5** 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 $mm^2$).

**TABLE 4: BMO-MRW, AGE 45 YEARS, BMO AREA 1.5 $MM^2$**

| | 1st percentile [µm] | 5th percentile [µm] |
|---|---|---|
| Global | 231 | 268 |
| Temporal | 146 | 177 |
| Temporal superior | 194 | 237 |
| Temporal inferior | 227 | 268 |
| Nasal | 246 | 291 |
| Nasal superior | 227 | 277 |
| Nasal inferior | 268 | 316 |

**TABLE 5: BMO-MRW, AGE 65 YEARS, BMO AREA 2.5 $MM^2$**

| | 1st percentile [µm] | 5th percentile [µm] |
|---|---|---|
| Global | 155 | 192 |
| Temporal | 94 | 124 |
| Temporal superior | 127 | 169 |
| Temporal inferior | 170 | 212 |
| Nasal | 146 | 192 |
| Nasal superior | 146 | 197 |
| Nasal inferior | 185 | 233 |

*RNFLT and BMO-MRW measurement precision for use of the ONH-RC scan pattern*
In a prospective, monocentric study the clinical precision of BMO-MRW and RNFLT measurements have been determined for use of the ONH-RC scan pattern.

34 subjects were enrolled into the study. Data of 32 subjects was included in analysis. 16 subjects had healthy eyes (healthy eyes without prior intraocular surgery except cataract surgery or laser in-situ keratomileusis, and without clinically significant vitreal, retinal or choroidal diseases, diabetic retinopathy, or disease of the optic nerve).

16 subjects had different stages of glaucomatous eyes (visual field mean deviation ranging from -0.5 to -25.8). All subjects' manifest spherical equivalent was between +6D and -6D, with astigmatism ≤ 2.0D.

Three qualified individuals, each operating one of three Spectralis devices equipped with the study software, performed the study device measurements. Each patient was measured thrice at each device in baseline and thrice in follow-up mode. Outcome metrics were repeatability and reproducibility of measurements of structural parameters of the optic nerve head (in particular, the neuroretinal rim of the ONH), and the peripapillary retinal nerve fiber layer. Additionally each patient was measured once (12° circle and BMO-MRW) with manually defined landmarks

(SPECTRALIS 5.6) to evaluate differences in results according to the different landmark positioning procedures.

In summary:

- 16 left and 16 right eyes were included.
- Average age of subjects was 57.7 years, ranging from 23 to 80 years.
- 50% of subjects were female, 50% male.
- Average refraction was -0.2 D (range -6.0 D to +4.75 D).

All acquired images were inspected by three experienced physicians for image quality (image quality index, missing scans, truncated scans, image defocus, floaters, pathologies and layer segmentation).

Manual correction of the fovea position was necessary in 11 of 288 APS definition activities (32 subjects x 9 definitions, 3 operators x 3 repeats). One subject had no distinguishable foveal pit and needed manual placement in 7 out of 9 definitions. The remaining 4 corrections are equally distributed between the healthy and glaucoma groups.

Manual correction of the BMO position was necessary in 51 of 288 APS definitions.

An overview over all corrections is shown in **Table 6**.

**TABLE 6: MANUAL CORRECTIONS OF FOVEA AND BMO POSITION DURING PRECISION DATA EVALUATION**

| Group | Fovea APS – manual correction | BMO APS – manual correction |
|---|---|---|
| Healthy | 2 of 144 (1.4%) | 22 of 144 (15.3%) |
| Glaucoma | 9 of 144 (6.3%) | 29 of 144 (20.1%) |
| All | 11 of 288 (3.8%) | 51 of 288 (17.7%) |

Typical causes of manual corrections of the BMO position are small discs, myopic eyes, tilted discs with external oblique border tissue, and other irregular BMO structures.

A random effect ANOVA with the effects operator (confounded with device) and eye were used for the analysis:

$$Y_{ijk} = \beta_0 + \beta_1 * \text{eye} + \beta_2 * \text{device} + \beta_3 * \text{device} * \text{eye} + e_{ijk}$$

where $Y_{ijk}$ stands for the repeated measurements, $\beta_0$ is the intercept and $\beta_i \sim N(0, \sigma_i^2)$ for $i \in \{1, 2, 3\} \in \{1, 2, 3\}$. and $e_{ijk}$ iid gaussian variables for the remaining variability. The variability of each component were estimated

The following **Table 7** and **Table 8** contain summary data of the analysis. For each endpoint and separate for the baseline and follow-up mode, the mean and the maximum of the repeatability and reproducibility coefficient of variation (CV) are tabulated.

**TABLE 7: MEAN CV OF THE ANOVA ANALYSIS**

| Mean CV | Repeatability | | Reproducibility | |
|---|---|---|---|---|
| | BL [%] | FU [%] | BL [%] | FU [%] |
| BMO-MRW | 1.65 | 1.24 | 1.93 | 1.86 |
| 3.5 mm | 2.71 | 1.03 | 3.38 | 3.11 |
| 4.1 mm | 2.68 | 1.35 | 3.39 | 3.33 |
| 4.7 mm | 2.92 | 1.53 | 3.60 | 3.33 |

**TABLE 8: MAXIMUM CV OF THE ANOVA ANALYSIS**

| Maximum CV | Repeatability | | Reproducibility | |
|---|---|---|---|---|
| | BL [%] | FU [%] | BL [%] | FU [%] |
| BMO-MRW | 2.98 | 2.43 | 3.45 | 3.12 |
| 3.5 mm | 3.86 | 1.65 | 5.14 | 5.04 |
| 4.1 mm | 4.11 | 2.06 | 4.95 | 5.63 |
| 4.7 mm | 4.22 | 2.84 | 5.38 | 4.90 |

The detailed results of the precision analysis for the BMO-MRW and the RNFLT circle measurements are shown in the following tables (**Table 9** to **Table 24**), separated for acquisitions in baseline and follow-up mode and for the different sub-groups (Normal and Glaucoma).

**TABLE 9: REPEATABILITY AND REPRODUCIBILITY FOR BMO-MRW - BASELINE MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 351.31 | 85.10 | 2.20 | 0.63 | 2.33 | 0.66 |
| T | 257.49 | 70.25 | 3.73 | 1.45 | 4.06 | 1.58 |
| TS | 326.74 | 78.98 | 4.60 | 1.41 | 4.85 | 1.48 |
| TI | 365.32 | 88.99 | 7.22 | 1.98 | 7.24 | 1.98 |
| N | 394.64 | 103.37 | 2.65 | 0.67 | 3.22 | 0.82 |
| NS | 381.16 | 99.30 | 5.32 | 1.40 | 5.38 | 1.41 |
| NI | 423.91 | 99.91 | 5.25 | 1.24 | 5.94 | 1.40 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 10: REPEATABILITY AND REPRODUCIBILITY FOR BMO-MRW - FOLLOW-UP MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 351.71 | 84.83 | 1.46 | 0.42 | 2.98 | 0.85 |
| T | 258.28 | 69.70 | 2.03 | 0.78 | 3.23 | 1.25 |
| TS | 327.16 | 77.54 | 3.21 | 0.98 | 5.23 | 1.60 |
| TI | 365.54 | 88.41 | 4.06 | 1.11 | 6.88 | 1.88 |
| N | 395.11 | 103.92 | 1.80 | 0.46 | 3.39 | 0.86 |
| NS | 380.80 | 99.32 | 4.14 | 1.09 | 6.85 | 1.80 |
| NI | 424.32 | 99.53 | 4.61 | 1.09 | 7.36 | 1.73 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 11: REPEATABILITY AND REPRODUCIBILITY FOR BMO-MRW - BASELINE MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 189.43 | 53.64 | 1.84 | 0.97 | 2.58 | 1.36 |
| T | 151.28 | 49.49 | 2.36 | 1.56 | 3.01 | 1.99 |
| TS | 158.88 | 66.63 | 4.52 | 2.85 | 5.46 | 3.44 |
| TI | 190.07 | 76.28 | 3.85 | 2.02 | 6.06 | 3.19 |
| N | 207.61 | 64.28 | 2.96 | 1.43 | 3.39 | 1.63 |
| NS | 196.98 | 64.54 | 5.87 | 2.98 | 6.79 | 3.45 |
| NI | 247.66 | 71.50 | 6.16 | 2.49 | 6.49 | 2.62 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 12: REPEATABILITY AND REPRODUCIBILITY FOR BMO-MRW - FOLLOW-UP MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 189.14 | 53.43 | 1.34 | 0.71 | 2.24 | 1.19 |
| T | 151.15 | 49.90 | 2.13 | 1.41 | 2.31 | 1.53 |
| TS | 158.77 | 65.93 | 3.43 | 2.16 | 4.39 | 2.77 |
| TI | 189.45 | 75.62 | 3.26 | 1.72 | 5.43 | 2.87 |
| N | 207.71 | 64.51 | 2.59 | 1.25 | 3.93 | 1.89 |
| NS | 196.29 | 64.56 | 4.77 | 2.43 | 6.12 | 3.12 |
| NI | 246.41 | 71.06 | 4.39 | 1.78 | 6.83 | 2.77 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 13: REPEATABILITY AND REPRODUCIBILITY FOR 3.5 MM CIRCLE SCAN PATTERN - BASELINE MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 98.62 | 9.59 | 1.09 | 1.10 | 2.10 | 2.13 |
| T | 66.42 | 11.91 | 1.48 | 2.22 | 1.69 | 2.55 |
| TS | 135.65 | 19.55 | 3.77 | 2.78 | 4.26 | 3.14 |
| TI | 133.71 | 14.90 | 2.80 | 2.10 | 3.11 | 2.32 |
| N | 81.35 | 12.03 | 2.18 | 2.68 | 3.23 | 3.96 |
| NS | 111.20 | 15.25 | 3.00 | 2.70 | 4.14 | 3.73 |
| NI | 112.88 | 18.00 | 3.39 | 3.00 | 4.80 | 4.26 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 14: REPEATABILITY AND REPRODUCIBILITY FOR 3.5 MM CIRCLE SCAN PATTERN - FOLLOW-UP MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 98.85 | 9.34 | 0.43 | 0.44 | 1.81 | 1.83 |
| T | 66.55 | 11.52 | 0.74 | 1.11 | 1.51 | 2.27 |
| TS | 136.34 | 19.63 | 1.16 | 0.85 | 4.09 | 3.00 |
| TI | 134.58 | 13.81 | 1.30 | 0.97 | 2.56 | 1.91 |
| N | 81.11 | 11.68 | 0.87 | 1.07 | 2.59 | 3.20 |
| NS | 111.26 | 14.88 | 0.96 | 0.86 | 3.83 | 3.44 |
| NI | 113.29 | 18.78 | 0.96 | 0.85 | 4.21 | 3.71 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 15: REPEATABILITY AND REPRODUCIBILITY FOR 3.5 MM CIRCLE SCAN PATTERN - BASELINE MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 66.22 | 19.62 | 1.09 | 1.65 | 1.41 | 2.13 |
| T | 50.50 | 15.27 | 1.39 | 2.76 | 1.81 | 3.59 |
| TS | 85.44 | 35.43 | 3.30 | 3.86 | 4.39 | 5.14 |
| TI | 91.06 | 36.84 | 2.95 | 3.24 | 2.95 | 3.24 |
| N | 51.70 | 13.71 | 1.61 | 3.11 | 1.70 | 3.28 |
| NS | 71.41 | 26.73 | 2.49 | 3.49 | 2.96 | 4.15 |
| NI | 77.44 | 26.04 | 2.48 | 3.20 | 2.82 | 3.64 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 16: REPEATABILITY AND REPRODUCIBILITY FOR 3.5 MM CIRCLE SCAN PATTERN - FOLLOW-UP MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 66.66 | 19.58 | 0.47 | 0.70 | 1.35 | 2.03 |
| T | 50.80 | 14.90 | 0.67 | 1.33 | 1.75 | 3.45 |
| TS | 85.96 | 35.05 | 1.24 | 1.44 | 4.33 | 5.04 |
| TI | 91.28 | 36.30 | 0.86 | 0.95 | 2.65 | 2.90 |
| N | 52.40 | 14.21 | 0.86 | 1.65 | 1.95 | 3.73 |
| NS | 71.55 | 26.84 | 0.76 | 1.06 | 2.23 | 3.11 |
| NI | 78.06 | 26.06 | 0.95 | 1.21 | 3.08 | 3.95 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 17: REPEATABILITY AND REPRODUCIBILITY FOR 4.1 MM CIRCLE SCAN PATTERN - BASELINE MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 84.54 | 7.68 | 0.90 | 1.06 | 1.62 | 1.91 |
| T | 59.37 | 10.05 | 1.25 | 2.11 | 1.61 | 2.72 |
| TS | 121.94 | 16.54 | 2.73 | 2.24 | 3.42 | 2.80 |
| TI | 120.50 | 11.88 | 2.63 | 2.18 | 3.01 | 2.50 |
| N | 66.52 | 9.17 | 1.63 | 2.45 | 2.30 | 3.45 |
| NS | 92.16 | 10.90 | 2.53 | 2.75 | 3.43 | 3.72 |
| NI | 89.91 | 14.23 | 2.44 | 2.71 | 3.35 | 3.73 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 18: REPEATABILITY AND REPRODUCIBILITY FOR 4.1 MM CIRCLE SCAN PATTERN - FOLLOW-UP MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 84.77 | 7.52 | 0.54 | 0.64 | 1.48 | 1.74 |
| T | 59.50 | 9.77 | 0.89 | 1.49 | 1.78 | 2.99 |
| TS | 122.28 | 16.21 | 1.05 | 0.86 | 2.99 | 2.45 |
| TI | 121.37 | 11.06 | 1.26 | 1.04 | 2.66 | 2.19 |
| N | 66.60 | 9.18 | 0.96 | 1.45 | 2.01 | 3.02 |
| NS | 92.00 | 10.64 | 1.19 | 1.29 | 3.64 | 3.96 |
| NI | 90.33 | 14.34 | 0.96 | 1.06 | 3.39 | 3.75 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 19: REPEATABILITY AND REPRODUCIBILITY FOR 4.1 MM CIRCLE SCAN PATTERN - BASELINE MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 58.73 | 16.13 | 0.97 | 1.66 | 1.16 | 1.98 |
| T | 46.73 | 12.59 | 1.92 | 4.11 | 2.31 | 4.95 |
| TS | 79.33 | 30.55 | 2.91 | 3.66 | 3.90 | 4.92 |
| TI | 83.30 | 34.62 | 2.16 | 2.60 | 2.38 | 2.85 |
| N | 45.02 | 10.41 | 1.42 | 3.16 | 1.55 | 3.45 |
| NS | 59.91 | 21.16 | 2.07 | 3.46 | 2.65 | 4.42 |
| NI | 63.80 | 20.33 | 2.13 | 3.35 | 2.55 | 4.00 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 20: REPEATABILITY AND REPRODUCIBILITY FOR 4.1 MM CIRCLE SCAN PATTERN - FOLLOW-UP MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 59.30 | 16.19 | 0.60 | 1.01 | 1.11 | 1.87 |
| T | 47.08 | 12.22 | 0.84 | 1.78 | 2.65 | 5.63 |
| TS | 80.28 | 30.84 | 1.06 | 1.32 | 3.70 | 4.61 |
| TI | 83.94 | 34.56 | 1.16 | 1.39 | 2.07 | 2.46 |
| N | 45.63 | 10.52 | 0.78 | 1.72 | 1.59 | 3.48 |
| NS | 60.47 | 21.54 | 1.08 | 1.78 | 2.57 | 4.25 |
| NI | 64.26 | 20.96 | 1.32 | 2.06 | 2.67 | 4.16 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 21: REPEATABILITY AND REPRODUCIBILITY FOR 4.7 MM CIRCLE SCAN PATTERN - BASELINE MODUS (NORMAL**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 74.16 | 6.85 | 0.95 | 1.28 | 1.37 | 1.85 |
| T | 54.69 | 8.99 | 1.59 | 2.92 | 1.68 | 3.07 |
| TS | 109.08 | 15.88 | 2.31 | 2.12 | 2.81 | 2.58 |
| TI | 110.83 | 10.09 | 2.11 | 1.90 | 2.64 | 2.38 |
| N | 56.71 | 7.47 | 1.29 | 2.27 | 1.85 | 3.27 |
| NS | 76.50 | 8.07 | 2.26 | 2.95 | 2.52 | 3.30 |
| NI | 74.09 | 12.46 | 2.49 | 3.36 | 2.96 | 4.00 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 22: REPEATABILITY AND REPRODUCIBILITY FOR 4.7 MM CIRCLE SCAN PATTERN - FOLLOW-UP MODUS (NORMAL)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 74.22 | 6.48 | 0.49 | 0.66 | 1.24 | 1.67 |
| T | 54.66 | 8.67 | 0.90 | 1.64 | 1.53 | 2.81 |
| TS | 108.81 | 15.85 | 0.89 | 0.82 | 2.50 | 2.30 |
| TI | 111.80 | 8.71 | 0.99 | 0.89 | 2.98 | 2.66 |
| N | 56.49 | 7.39 | 0.82 | 1.45 | 2.04 | 3.61 |
| NS | 76.51 | 7.80 | 1.07 | 1.40 | 2.18 | 2.84 |
| NI | 74.34 | 12.57 | 0.94 | 1.26 | 2.26 | 3.04 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 23: REPEATABILITY AND REPRODUCIBILITY FOR 4.7 MM CIRCLE SCAN PATTERN - BASELINE MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 52.75 | 13.81 | 0.91 | 1.72 | 1.20 | 2.27 |
| T | 43.49 | 11.16 | 1.77 | 4.07 | 2.15 | 4.94 |
| TS | 73.64 | 28.49 | 2.77 | 3.76 | 3.92 | 5.32 |
| TI | 75.96 | 30.90 | 2.36 | 3.11 | 2.59 | 3.41 |
| N | 40.23 | 8.18 | 1.42 | 3.52 | 1.63 | 4.06 |
| NS | 51.60 | 16.79 | 2.18 | 4.22 | 2.78 | 5.38 |
| NI | 53.35 | 15.21 | 1.96 | 3.68 | 2.42 | 4.53 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

**TABLE 24: REPEATABILITY AND REPRODUCIBILITY FOR 4.7 MM CIRCLE SCAN PATTERN - FOLLOW-UP MODUS (GLAUCOMA)**

| | | | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|
| | **Mean [µm]** | **SD[µm]** | **SD [µm]** | **CV [%]** | **SD [µm]** | **CV [%]** |
| G | 53.17 | 13.74 | 0.52 | 0.97 | 1.13 | 2.13 |
| T | 43.53 | 11.05 | 0.87 | 2.00 | 2.13 | 4.90 |
| TS | 74.24 | 28.26 | 1.54 | 2.08 | 3.31 | 4.46 |
| TI | 76.63 | 30.69 | 1.45 | 1.89 | 3.02 | 3.95 |
| N | 40.74 | 8.17 | 0.72 | 1.76 | 1.42 | 3.50 |
| NS | 51.90 | 16.77 | 0.87 | 1.69 | 2.13 | 4.11 |
| NI | 54.04 | 15.58 | 1.53 | 2.83 | 2.51 | 4.64 |

All statistics are estimated from a two-way random effect ANOVA model (REML) with the random effects operator (confounded with device) and eye.
Mean is the intercept of the ANOVA model.
SD is the standard deviation of the measurement.
Repeatability-SD is the square root of the residual variance.
Repeatability-Limit is 2.8 x Repeatability-SD.
Repeatability-CV is Repeatability-SD/Mean*100% (COV).
Reproducibility-SD is the square root of the sum of the operator variance, the interaction variance, and the residual variance.
Reproducibility-Limit is 2.8 x Reproducibility-SD.
Reproducibility-CV is Reproducibility-SD/Mean*100% (COV).

*Limit of Agreement BMO center position*

To evaluate potential differences according to the different landmark positioning procedures the results of the 12° circle scan pattern with the manually defined landmarks (SPECTRALIS 5.6) and the 3.5 mm circle scan pattern with the APS semi-automated defined landmarks (SPECTRALIS 6.0) are compared. The following **Table 25** and **Table 26** summarize the results, the results derived from both measurements agree.

**TABLE 25: LIMIT OF AGREEMENT SUMMARY OF RNFLT 3.5MM CIRCLE SCAN PATTER USING APS WITH MANUAL POSITIONED 12° CIRCLE SCAN PATTERN-NORMAL SUBJECTS**

| | Mean Diff [µm] | Mean Diff [%] | Min Diff [µm] | Max Diff [µm] | SD [µm] | LOA low [µm] | LOA up [µm] |
|---|---|---|---|---|---|---|---|
| G | -0.6 | -0.5 | -10.4 | 7.2 | 5.4 | -11.1 | 10.0 |
| T | 0.5 | 0.8 | -6.0 | 6.1 | 3.4 | -6.3 | 7.2 |
| TS | 1.9 | 1.5 | -15.7 | 21.6 | 7.8 | -13.5 | 17.3 |
| TI | -0.4 | -0.3 | -12.4 | 10.3 | 6.2 | -12.6 | 11.7 |
| N | -2.6 | -2.4 | -22.2 | 10.6 | 8.2 | -18.6 | 13.5 |
| NS | -1.0 | -0.2 | -18.3 | 13.8 | 10.3 | -21.2 | 19.3 |
| NI | 0.5 | 0.7 | -20.4 | 18.2 | 10.3 | -19.6 | 20.7 |

Mean of the differences (measurement - predicate)
Mean of the percentile differences, with respect to the predicate
Minimum of the differences
Maximum of the differences
Standard deviation of the differences
Lower LOA = Mean - 1.96 standard deviation
Upper LOA = Mean + 1.96 standard deviation

**TABLE 26: LIMIT OF AGREEMENT SUMMARY OF RNFLT 3.5MM CIRCLE SCAN PATTERN USING APS WITH MANUAL POSITIONED 12° CIRCLE SCAN PATTERN - GLAUCOMA SUBJECTS**

| | Mean Diff [µm] | Mean Diff [%] | Min Diff [µm] | Max Diff [µm] | SD [µm] | LOA low [µm] | LOA up [µm] |
|---|---|---|---|---|---|---|---|
| G | 1.1 | 1.2 | -4.2 | 10.7 | 3.8 | -6.4 | 8.6 |
| T | 0.7 | 0.8 | -3.0 | 9.0 | 2.9 | -4.9 | 6.3 |
| TS | 1.9 | 3.8 | -7.1 | 15.7 | 5.5 | -8.8 | 12.6 |
| TI | 1.3 | 0.6 | -6.0 | 8.2 | 4.7 | -7.9 | 10.5 |
| N | 0.6 | 0.8 | -6.7 | 9.7 | 4.0 | -7.1 | 8.4 |
| NS | 3.1 | 5.4 | -8.2 | 22.1 | 8.7 | -14.0 | 20.2 |
| NI | 0.7 | -0.1 | -10.8 | 15.2 | 7.0 | -12.9 | 14.4 |

Mean of the differences (measurement - predicate)
Mean of the percentile differences, with respect to the predicate
Minimum of the differences
Maximum of the differences
Standard deviation of the differences
Lower LOA = Mean - 1.96 standard deviation
Upper LOA = Mean + 1.96 standard deviation

*RNFLT and BMO-MRW measurement agreement with the predicate device*

In a prospective, monocentric study the measurement agreement between BMO-MRW and RNFLT measurements with an OCT based landmark definition process and RNFLT measurements with an infrared image based landmark definition process has been determined. 48 subjects were enrolled into the study. Data of 40 subjects were included in analysis.

20 subjects had healthy eyes (healthy eyes without prior intraocular surgery except cataract surgery or laser in-situ keratomileusis, and without clinically significant vitreal, retinal or choroidal diseases, diabetic retinopathy, or disease of the optic nerve).

20 subjects had different stages of glaucomatous eyes (visual field mean deviation ranging from -0.02 to -31.95). All subjects' manifest spherical equivalent was in between +6D and -6D, with astigmatism ≤ 2.0D.

The study aimed to evaluate the agreement of structural parameters of the optic nerve head (ONH), in particular, the neuroretinal rim of the ONH, and the peripapillary retinal nerve fiber layer based on infrared (IR) image-based (Fovea-to-Disc-Alignment technology - FoDi) and optical coherence tomography (OCT) (Anatomic positioning System – APS) based scan alignment. All subjects were examined once with each device version and underwent further supporting diagnostics.
In summary:

- 20 left and 20 right eyes were included.
- Average age of subjects was 56.3 years, ranging from 23 to 81 years.
- 50% of subjects were female, 50% male.
- Average refraction was -0.79 D (range -5.25 D to +3.50 D).

All acquired images were inspected by the investigator for image quality (image quality index, missing scans, truncated scans, image defocus, floaters, pathologies, scan center position alignment, and layer segmentation).

To test agreement of parameters of the optic nerve head and the peripapillary retinal nerve fiber layer measurements acquired with the different alignment methods and circle characteristics, the following statistic are calculated

- The mean of the differences (measurement – predicate),
- the minimum and maximum difference,
- the standard deviation of the differences,
- the 95% limits of agreement (LOA)

All differences between the different RNFLT scans are overall small and within expected ranges and below predefined thresholds. Therefore results derived from the predicate software version 5.6 and the subject device software version 6.0 are considered to agree.

The following **Table 27** and **Table 28** show the detailed agreement data for the comparison between RNFL thickness measurements from the 3.5 mm circle scan and RNFL thickness measurements from the 12° circle scan of the predicate device (software version 5.6). The global and sector values are tabulated separate for the sub-groups (Normal and Glaucoma).

**TABLE 27: LIMIT OF AGREEMENT SUMMARY OF RNFLT 3.5 MM CIRCLE SCAN PATTERN WITH THE 12° CIRCLE SCAN PATTERN- NORMAL SUBJECTS**

| | Mean Diff [µm] | Mean Diff [%] | Min Diff [µm] | Max Diff [µm] | SD [µm] | LOA low [µm] | LOA up [µm] |
|---|---|---|---|---|---|---|---|
| G | 4.5 | 4.7 | -1.6 | 13.4 | 4.5 | -4.2 | 13.2 |
| T | -1.0 | -0.8 | -12.0 | 12.8 | 5.1 | -11.0 | 9.1 |
| TS | 4.7 | 3.6 | -12.1 | 26.9 | 8.1 | -11.3 | 20.6 |
| TI | 4.2 | 3.0 | -6.1 | 18.6 | 7.1 | -9.8 | 18.1 |
| N | 6.6 | 10.5 | -7.4 | 22.8 | 7.2 | -7.4 | 20.7 |
| NS | 6.4 | 5.9 | -6.1 | 22.7 | 9.0 | -11.4 | 24.1 |
| NI | 9.3 | 9.7 | -25.9 | 33.9 | 11.9 | -13.9 | 32.6 |

Mean of the differences (measurement - predicate)
Mean of the percentile differences, with respect to the predicate
Minimum of the differences
Maximum of the differences
Standard deviation of the differences
Lower LOA = Mean - 1.96 standard deviation
Upper LOA = Mean + 1.96 standard deviation

**TABLE 28: LIMIT OF AGREEMENT SUMMARY OF RNFLT 3.5 MM CIRCLE SCAN PATTER WITH THE 12° CIRCLE SCAN PATTER - GLAUCOMA SUBJECTS**

| | Mean Diff [µm] | Mean Diff [%] | Min Diff [µm] | Max Diff [µm] | SD [µm] | LOA low [µm] | LOA up [µm] |
|---|---|---|---|---|---|---|---|
| G | 3.7 | 6.7 | -5.5 | 13.5 | 5.4 | -6.8 | 14.3 |
| T | -0.2 | 0.8 | -25.5 | 7.4 | 6.7 | -13.2 | 12.9 |
| TS | 7.0 | 12.2 | -3.2 | 42.9 | 11.8 | -16.2 | 30.2 |
| TI | 1.3 | 1.9 | -14.9 | 23.3 | 8.2 | -14.8 | 17.4 |
| N | 3.3 | 12.0 | -20.6 | 28.8 | 11.4 | -18.9 | 25.6 |
| NS | 10.0 | 30.1 | -5.5 | 50.3 | 13.9 | -17.2 | 37.2 |
| NI | 5.2 | 9.9 | -5.7 | 16.8 | 5.7 | -5.9 | 16.4 |

Mean of the differences (measurement - predicate)
Mean of the percentile differences, with respect to the predicate
Minimum of the differences
Maximum of the differences
Standard deviation of the differences
Lower LOA = Mean - 1.96 standard deviation
Upper LOA = Mean + 1.96 standard deviation

## VIII. Conclusions

The SPECTRALIS HRA+OCT has the same Intended Use as the predicate device. The basic technological characteristics remain the same, and the device has been updated to include a new reference database that includes optic nerve head (ONH) neuroretinal rim width measurements in addition to retinal nerve fiber layer (RNFL) thickness. The method for locating the fovea and the optic disc center were modified to result in a more accurate definition of both locations with the revised imaging software. An additional imaging function, Enhanced Depth Imaging (EDI), is added to enhance viewing the deep structures of the eye. These differences do not affect safety or effectiveness, as verified with clinical and bench testing and software verification and validation. Therefore, it is concluded that the SPECTRALIS HRA+OCT is substantially equivalent to the predicate device.

Two optional accessory lenses have been added to allow the user to view a greater proportion of the posterior eye in one view: the Wide Field Objective and the Ultra-Widefield Objective. These lenses are similar to two reference devices, Nidek Ophthalmoscope F-10 (K072259) and Optos 200T (K111628) and do not raise new issues of safety and effectiveness.