K101505

510(k) Summary

Optovue, Inc.
RTVue with Normative Database

SEP 15 2010

This 510(k) summary for the RTVue with Normative Database is submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

General Information

Manufacturer:

Optovue, Inc.
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Device Information

Classification: Class II

Trade Name: RTVue with Normative Database

Common Name: Optical Coherence Tomography (OCT)

Classification Name: Ophthalmoscope, a-c powered (21 CFR§ 886.1570)

Predicate Device

(1) RTVue with CA (K071250) – Manufactured by Optovue, Inc.
(2) StratusOCT with RNFL & Macula Normative Database (K033123) – manufactured by Carl Zeiss Meditec, Inc.

Intended Use

The RTVue with Normative Database is an optical coherence tomography system indicated for the in-vivo imaging and measurement of the retina, retinal nerve fiber layer, and optic disc as an aid in the diagnosis and management of retinal disease. The RTVue with Normative Database is also a

quantitative tool for the comparison of retina, retinal nerve fiber layer, and optic disc measurements in the human eye to a database of known normal subjects. It is intended for use as a diagnostic device to aid in the detection and management of ocular diseases.

Device Description

The RTVue is a computer controlled ophthalmic imaging and measurement system that employs optical coherence tomography to image and measure the posterior segment of the eye. The device is currently cleared for in vivo imaging and measurement of the various retinal layers (K062552). Imaging and measurements include but are not limited to the internal limiting membrane (ILM), the retinal nerve fiber layer (RNFL), the ganglion cell complex (GCC), the retinal pigment epithelium (RPE), the outer retinal thickness, the total retinal thickness and optic disk structures including the cup and neuroretinal rim as an aid in the diagnosis and management of retinal disease. The measurements for the ILM and RPE are height measurements relative to the RPE reference plane. The RNFL, GCC, the outer retinal thickness and total retinal thickness are thickness measurements where RNFL is the thickness of the RNFL layer, the GCC is the thickness from the ILM to the inner plexiform layer (IPL), the outer retinal thickness is the thickness from the IPL to the RPE, and total retinal thickness is the thickness from the ILM to the RPE. The current submission is for a software modification to add a normative database. With the additional normative database (NDB), the RTVue can compare the measured data from the GCC, the RNFL, the full retinal thickness, optic disc cup and optic disc rim measurements to the normative database. The RTVue with Normative Database provides a statistical reference of the GCC, the RNFL, the full retinal thickness, optic disc cup and optic disc rim measurements to a database of known normal subjects. The RTVue with Normative Database will provide the analysis information to be used as a clinical reference to aid in the diagnosis and management of ocular diseases.

Substantial Equivalence

The RTVue with Normative Database is substantially equivalent to the predicate device identified previously. The RTVue is similar to the previously cleared RTVue device with regard to intended use, operating principle, function, material, and energy source. Technological comparisons and clinical testing demonstrate that the RTVue with Normative Database is functionally equivalent to the predicate devices.

Performance Data

Clinical data was collected and evaluated to support the intended use for the RTVue with Normative Database and to demonstrate substantial equivalence to the predicate devices.

Description of Precision Study, Subject Selection Criteria and Pathologies

Instrument:
Three RTVue (K062552) with three different operators were used in this study. Measurements results of various structures within the eye including retinal thickness, RNFL thickness, optic disc measurements, and Ganglion Cell Complex (GCC) measurements were compared in normal eyes, and eyes with retina pathology and glaucoma.

Scans:
The RTVue device has three scan patterns where measurements are compared to a normative database. These scans include the 1) EMM5 scan, 2) the ONH scan, and 3) the GCC scan. The

EMM5 scan is centered on the fovea and provides measurements of the full retina thickness and the inner retina thickness. Only the full retina thickness measurements are compared to the normative database. This scan can be used to assess possible retina pathologies. The ONH scan is centered on the optic disc and provides measurements of the RNFL and optic disc. This scan can be used to assess possible glaucoma. The GCC scan is centered at 1 mm off from the fovea in order to cover more temporal retina area. It provides measurements of the inner retina layers that contain the ganglion cell axon (RNFL), cell body, and dendrite (inner plexiform layer). This scan can be used to assess glaucoma. Both eyes were scanned in each subject.

Subjects:
1) Normal healthy eyes with no ocular pathology, 2) glaucoma patients and, 3) retina patients were enrolled in the study at two clinical sites. Normal subjects were free from ocular pathology as determined by the Principal Investigator (PI) at each clinical site. Glaucoma patients were diagnosed as having glaucoma by the PI at each site. Retina patients included subjects with any type of retina pathology diagnosed by the PI. Retina pathologies included but were not limited to, AMD, DME, and ERM. There were 4 normal subjects, 4 retina patients, and 4 glaucoma patients enrolled for each RTVue devices. There were 3 RTVue devices at 2 clinical sites. At one site, there were 2 RTVues systems and 2 operators at different times. In total, there were 12 subjects enrolled for each of the 3 RTVue devices; a total of 36 subjects were used from the study.

Selection Criteria:
All data was carefully reviewed for completeness and quality in two levels, namely, the subject level and the individual scan level. At the subject level, the CRF was carefully reviewed to qualify each subject against all inclusion and exclusion criteria by comparing the study protocol with the CRF. At the individual scan level, the data was reviewed for quality to ensure data meeting inclusion criteria was accepted.

In a clinical environment, only scans with acceptable quality should be used. In order to match our analysis with acceptable clinical results, we reviewed and excluded all scans in the study with poor image quality. Image quality is based on a number of factors, including overall signal strength, localized weak signals, eye blink, data out of boundary, and data off-center. Due to the selection criteria, the sample size for each scan type varies.

Precision Results

The following tables provide the precision results for the scans with RTVue with Normative Database with both eyes combined. The data in the tables include the number of scans per subject group, the overall mean, the standard deviation, the repeatability standard deviation (median value of subfields with the minimum subfield value and the maximum subfield value), and reproducibility standard deviation (median value of subfields with the minimum subfield value and the maximum subfield value).

i) EMM5 Scan Results (Normal and Retina Patients)

The following tables show the overall precision results with the EMM5 scan for full retinal thickness in the fovea for normals and retina patients.

EMM5 Full Retina Fovea			
	Normal Patients	Retina Patients	Glaucoma Patients

# of Scans	71	71	71
Overall Mean (Overall SD)	243.61 (26.00)	267.15 (73.32)	246.22 (22.14)
Repeatability SD* (Min, Max)	2.57(1.66, 2.57)	2.96(1.83, 3.15)	3.01(1.95, 3.01)
Reproducibility SD** (Min, Max)	17.72(1.66, 17.72)	13.78(1.83, 13.78)	3.01(2.05, 5.80)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.

**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the EMM5 scan for full retinal thickness in the periphery (average over 8 sectors outside the fovea) for normals and retina patients.

EMM5 Full Retina Thickness Peripheral Results			
	Normal Patients	Retina Patients	Glaucoma Patients
# of Scans	71	71	71
Overall Mean (Overall SD)	295.05 (16.21)	299.03 (30.70)	282.30 (25.26)
Repeatability SD* (Min, Max)	1.96(1.66, 2.57)	2.69(1.83, 3.15)	2.35(1.95, 3.01)
Reproducibility SD** (Min, Max)	2.01(1.66, 17.72)	2.69(1.83, 13.78)	2.66(2.05, 5.80)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.

**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

ii) ONH Scan Results (Normals and Glaucoma Patients)

The following tables show the overall precision results with the ONH scan for average RNFL thickness for normals and glaucoma patients.

ONH Average RNFL		
	Normal Patients	Glaucoma Patients
# of Scans	72	72
Overall Mean (Overall SD)	100.82 (8.11)	86.40 (14.99)
Repeatability SD* (Min, Max)	1.76(1.76, 6.18)	1.56(1.56, 5.86)
Reproducibility SD** (Min, Max)	2.11(2.11, 9.78)	7.87(3.92, 16.33)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.

**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the ONH scan for the average over 2 hemi-spheres, 4 quadrants, and 8 sectors for normals and glaucoma patients.

ONH RNFL averaged over 2 Hemispheres, 4 Quadrants, 8 Sectors		
	Normal Patients	Glaucoma Patients
# of Scans	72	72
Overall Mean (Overall SD)	100.82 (14.80)	86.41 (18.55)

Repeatability SD* (Min, Max)	3.92(1.76, 6.18)	4.48(1.56, 5.86)
Reproducibility SD** (Min, Max)	5.40(2.11, 9.78)	7.84(3.92, 16.33)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.
**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the ONH scan for the cup area measurement for normals and glaucoma patients.

ONH Cup Area		
	Normal Patients	Glaucoma Patients
# of Scans	72	72
Overall Mean (Overall SD)	0.39 (0.18)	1.04 (0.53)
Repeatability SD* (Min, Max)	0.02 (0.02, 0.03)	0.07(0.07, 0.21)
Reproducibility SD** (Min, Max)	0.02 (0.02, 0.03)	0.07(0.07, 0.21)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.
**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the ONH scan for the rim area measurement for normals and glaucoma patients.

ONH Rim Area		
	Normal Patients	Glaucoma Patients
# of Scans	72	72
Overall Mean (Overall SD)	0.69 (0.17)	0.89 (0.66)
Repeatability SD* (Min, Max)	0.03 (0.02, 0.03)	0.18(0.07, 0.21)
Reproducibility SD** (Min, Max)	0.03 (0.02, 0.03)	0.18(0.07, 0.21)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.
**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the ONH scan for the vertical CD ratio measurement for normals and glaucoma patients.

ONH Vertical CD Ratio		
	Normal Patients	Glaucoma Patients
# of Scans	72	72
Overall Mean (Overall SD)	2.15 (0.65)	0.76 (0.23)
Repeatability SD* (Min, Max)	0.01 (0.01, 0.04)	0.05(0.05, 0.08)
Reproducibility SD** (Min, Max)	0.01 (0.01, 0.04)	0.05(0.05, 0.08)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.

**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

iii) GCC Scan Results (Normals and Glaucoma Patients)

The following tables show the overall precision results with the GCC scan for the inner retina average for normals and glaucoma patients.

GCC Inner Retina Average		
	Normal Patients	Glaucoma Patients
# of Scans	72	71
Overall Mean (Overall SD)	98.28 (9.31)	81.76 (8.90)
Repeatability SD* (Min, Max)	1.86 (1.86, 2.07)	1.18 (1.18, 1.59)
Reproducibility SD** (Min, Max)	7.56 (7.32, 7.92)	2.55 (1.59, 3.36)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.
**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the GCC scan for the FLV thickness measurement for normals and glaucoma patients.

GCC GCC FLV		
	Normal Patients	Glaucoma Patients
# of Scans	72	71
Overall Mean (Overall SD)	0.60 (0.67)	4.30 (3.47)
Repeatability SD* (Min, Max)	0.37 (0.37, 0.37)	0.88 (0.88, 0.88)
Reproducibility SD** (Min, Max)	0.46 (0.46, 0.46)	1.04 (1.04, 1.04)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.
**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

The following tables show the overall precision results with the GCC scan for the GLV thickness measurement for normals and glaucoma patients.

GCC GCC GLV		
	Normal Patients	Glaucoma Patients
# of Scans	72	71
Overall Mean (Overall SD)	3.99 (3.43)	15.51 (7.81)
Repeatability SD* (Min, Max)	0.83 (0.83, 0.83)	1.03 (1.03, 1.03)
Reproducibility SD** (Min, Max)	2.44 (2.44, 2.44)	1.71 (1.71, 1.71)

*estimate of the standard deviation among measurements taken on the same subject using the same operator and device in the same testing session with repositioning.

**estimate of the standard deviation among measurements taken on different subjects using different operators and devices, including repeatability; in some cases the maximum reproducibility estimates were impacted by mean thickness difference between subjects in different sites.

Registration Results

Image registration using blood vessel matching is used for both the EMM5 scan and the ONH scan. The image registration algorithm uses a reference image to register all scans based on matching detected blood vessel patterns. For this internal validation study, we performed both an accuracy test as well as a precision test in order to evaluate the efficacy of the blood vessel registration method.

The following tables show the values at 2 times the standard deviation values for each parameters for these two scan types.

EMM5	FRT Fovea	FRT Para Tempo	FRT Para Superior	FRT Para Nasal	FRT Para Inferior	FRT Peri Tempo	FRT Peri Superior	FRT Peri Nasal	FRT Peri Inferior
	6.345	3.9121	4.6186	3.6347	2.795	5.568	5.669	4.772	3.63

ONH	TU	ST	SN	NU	NL	IN	IT	TL
	9.8	10.0	9.6	9.6	8.0	9.8	8.0	5.6

Normative Databases

The normative data was collected at 11 clinical sites following an IRB approved protocol and enrolled known healthy eyes from 480 individuals (over 640 eyes) with a wide age range (18-84) from various ethnic backgrounds including 33% Caucasians, 22% Asians, 20% African Americans, 12% Hispanics, 12% Indian, and 1% other, approximately. Normative databases are adjusted by age, signal strength and disc area (where applicable), not by axial length, refraction or any other parameters. The normative limits do not take into account differences that may be present due to ethnicity.

In our clinical studies, the repeatability and reproducibility were found to be very good and were found to be similar for normal groups and pathology groups. We believe the Normative Database is a good representation of the patient population because it was created from a large population of patients from 11 clinical sites worldwide. Ocular measurements taken by the RTVue have been compared to other OCT devices by renowned leaders in the field of Ophthalmology and found to have good repeatability and reproducibility[1-5].

Conclusion

As described in this 510(k) Summary, all testing and analysis were completed on the RTVue with Normative Database to ensure that the device is safe and effective for its intended.

1. Tan O, Chopra V, Lu A, Schuman J, Ishikawa H, Wollstein G, Varma R, Huang D. Detection of macular ganglion cell loss in glaucoma by Fourier-Domain Optical Coherence Tomography. Ophthalmol. 2009; 116:2305-2314.
2. González-Garcia AO, Vizzeri G, Bowd C, Medeiros FA, Zangwill LM, Weinreb RN.Reproducibility of RTVue Retinal Nerve Fiber Layer Thickness and Optic Disc Measurements and Agreement with Stratus Optical Coherence Tomography Measurements. Am J Ophthalmol. 2009 Mar 5.
3. Garas A, Vargha P, Hollo G. Reproducibility of retinal nerve fiber layer and macular thickness measurement with the RTVue-100 optical coherence tomography. Ophthalmol. 2010; 117: 738-746.
4. Garas A, Toth M, Vargha P, Hollo G. Comparison of repeatability of retinal nerve fiber layer thickness measurement made with the RTVue Fourier-domain Optocal Coherence Tomograph and the GDx Scanning Laser Polarimeter with Variable or Enhanced Cornea Compensation. J Glaucoma. 2009; Oct.
5. Sehi M, Grewal DS, Sheets CW, Greenfield DS. Diagnostic ability of Fourier-domain vs time-domain optical coherence tomography for glaucoma detection. Am J Ophthalmol. 2009; 148: 597-605.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-G609
Silver Spring, MD 20993-0002

Optovue, Inc
c/o Mr. John Talarico
VP Regulatory and Clinical Affairs
45531 Northport Loop W.
Fremont, CA 94538

SEP 15 2010

Re: K101505
Trade/Device Name: RTVue with Normative Database
Regulation Number: 21 CFR 886.1570
Regulation Name: Ophthalmoscope
Regulatory Class: Class II
Product Code: HLI
Dated: August 12, 2010
Received: August 19, 2010

Dear Mr. Talarico:

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 go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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 Small Manufacturers, International and Consumer Assistance 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,

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

Enclosure

Indications for Use

510(k) Number (if known): K101505

SEP 15 2010

Device Name: RTVue with Normative Database

Indications For Use:

The RTVue with Normative Database is an optical coherence tomography system indicated for the in vivo imaging and measurement of the retina, retinal nerve fiber layer, and optic disk as an aid in the diagnosis and management of retinal disease. The RTVue with Normative Database is also a quantitative tool for the comparison of retina, retinal nerve fiber layer, and optic disk measurements in the human eye to a database of known normal subjects. It is intended for use as a diagnostic device to aid in the detection and management of ocular diseases.

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Ophthalmic, Neurological and Ear,
Nose and Throat Devices

510(k) Number K101505