DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

June 9, 2017

Optovue, Inc.
Edward J. Sinclair
Vice President, Regulatory and Quality Affairs
2800 Bayview Drive
Fremont, CA 94538

Re: K163475
Trade/Device Name: iVue
Regulation Number: 21 CFR 886.1570
Regulation Name: Ophthalmoscope
Regulatory Class: Class II
Product Code: OBO, HLI
Dated: May 5, 2017
Received: May 8, 2017

Dear Edward J. Sinclair:

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,

Denise L. Hampton -S

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)*

K163475

Device Name

iVue

Indications for Use *(Describe)*

The iVue is a non-contact, high resolution tomographic imaging device. It is intended for in-vivo imaging, axial cross-sectional, and three-dimensional imaging and measurement of anterior and posterior ocular structures, including retina, retinal nerve fiber layer, ganglion cell complex (GCC), optic disc, cornea, corneal epithelia, corneal stroma and anterior chamber of the eye. With the integrated normative database, the iVue is a quantitative tool for the comparison of retina, retinal nerve fiber layer, ganglion cell complex, and optic disc measurements to a database of known normal subjects. The iVue is indicated for use as a device to aid in the diagnosis, documentation, and management of ocular health and diseases in the adult population.

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)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) SUMMARY

Submitter Information

Company:	Optovue, Inc. 2800 Bayview Drive Fremont, CA 94538 Phone: (510) 623-8868 Fax: (510) 651-2516 Est. Registration No.: 3005950902
Contact Person:	Edward J. Sinclair Vice President, Regulatory and Quality Affairs Phone: (510) 897-1575 Fax: (510) 651-2516
Date Prepared:	June 8, 2017

Device Name and Classification

Common Name:	Optical Coherence Tomography System
Proprietary Name:	iVue
Classification Name:	Tomography, Optical Coherence
Product Code:	OBO, HLI
Regulation Number:	21 CFR§ 886.1570
Device Class:	II

Predicate Device

Company:	Optovue, Inc.
Device:	iVue with Normative Database (K121739)

Intended Use

The iVue is an optical coherence tomography system intended for *in vivo* imaging, axial cross-sectional, three-dimensional imaging and measurement of anterior and posterior ocular

structures. There is no change in the intended use between the predicate iVue device and the modified iVue device that is the subject of this submission.

Indications For Use

Optovue has updated the iVue *indications for use* based on the modified ability of the software to determine the corneal epithelia and stroma layer thickness. The epithelia and stroma have been added to the current list of ocular structures that can be imaged by the iVue device. The complete, updated indication statement is provided below:

The iVue is a non-contact, high resolution tomographic imaging device. It is intended for in vivo imaging, axial cross-sectional, and three-dimensional imaging and measurement of anterior and posterior ocular structures, including retina, retinal nerve fiber layer, ganglion cell complex (GCC), optic disc, cornea, corneal epithelia, corneal stroma and anterior chamber of the eye. With the integrated normative database, the iVue is a quantitative tool for the comparison of retina, retinal nerve fiber layer, ganglion cell complex, and optic disc measurements to a database of known normal subjects. The iVue is indicated for use as a device to aid in the diagnosis, documentation, and management of ocular health and diseases in the adult population.

Device Description

The iVue is used to capture, store, display and print spectral domain-optical coherence tomography (SD-OCT) images of the posterior and anterior structure of the eye. The device software includes a Normative Database (NDB), consisting of OCT data from a range of known normal subjects that can be used to compare a new patient's measurements in relation to the normal distribution.

iVue is a computer-controlled ophthalmic imaging system using either a laptop computer or "All-in-One" computer. For laptop systems there are two control box options of 120 or 230 volts. The control box interfaces between the motorized table column and the medical-grade power supply for the computer.

<u>iVue System Key Functional Components</u>
The iVue system contains the following hardware components:

- **Scanner Head:** the scanner is the main component of the iVue system. It is used to view and scan the patient's eye, collect the OCT signal, and send it to the computer for processing.
- **Computer:** the system computer, either a laptop or All-in-One ("AIO"), which includes the computer and monitor in one unit), is approved for medical use. It supports scanner operation and processes, stores and displays exam data through the application software. The searchable iVue database stores and organizes patient and exam data.
- **Control Box***:* the control box supports operation of the scanner and contains the backup hard disk.
- **Joystick and Chinrest Assembly***:* the joystick moves the scanner left and right, forward and back, and aligns it with the patient's eye to capture the scan.

- **Footswitch (optional)***:* the footswitch provides another way to capture scans, including auto-adjustment, capture and saving.
- **Motorized Table (optional)**: a motorized table is optional. Customers may order the table in two input voltages of 120V or 230V.
- **Cornea Adapter Module:** the cornea lens adapter is attached to the front of the instrument to enable the iVue to image the cornea and anterior chamber of the eye.

Comparison of Technological Characteristics with the Predicate Device

The iVue with modified software is substantially equivalent to the iVue predicate device (cleared by FDA in K121739 on January 18, 2013). The intended use, mechanism of action, subassemblies, and key components remain the same. The modified software uses equivalent optical coherence tomography and segmentation technology as the predicate. The iVue device has been updated in the following ways:

1. A software modification allows automated segmentation of the posterior corneal epithelium boundary to provide the thickness of the epithelial layer. This capability, in conjunction with previously-cleared full cornea thickness measurement (i.e., "pachymetry"), also allows the software to automatically calculate the thickness of the stroma layer. Previously, the thickness of the epithelial and stroma layers could be manually measured using digital calipers in the iVue software. Consequently, the proposed software changes will automate the manual process of measuring the corneal epithelium and stroma layer thickness that could be performed using the previously cleared iVue software and provide color thickness "maps" of those layers.

2. There were several changes to the iVue device that did not require 510(k) premarket clearance when made. These include changing the Line Scan Camera communication from gigabit Ethernet to USB 3, removal of redundant LCD monitor from the scanner head, addition of an "All-in-One" computer option, support for Windows 7 operating system, updated reports and other minor software changes.

Risk Analysis

The risk management process at Optovue complies with EN ISO 14971:2012 *"Medical devices -- Application of risk management to medical devices."* As required by this standard, risk analyses are conducted according to defined procedures, using experienced, qualified personnel from multiple functions throughout the organization with prior experience in risk assessment.

The iVue Hazard Analysis was updated by the same qualified personnel who re-assessed the device with respect to all changes. Potential hazards were mitigated through the device design, software controls and user instructions and any mitigations were subsequently verified and validated. All of the identified hazards were mitigated to an acceptable level of risk. The potential benefits to patients outweigh the low residual risk after modifying the iVue software to enable automated thickness measurement of the corneal epithelia and stroma layers.

Performance Data

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

Electrical Safety and Electromagnetic Compatibility (EMC)
The iVue device has been tested according to IEC 60601-1 and IEC 60601-1-2 standards and was found to meet all requirements.

Software Verification and Validation Testing
Device software was verified and validated to support the indications for use according to IEC 62304:2006 "*Medical device software – Software life cycle processes"* and FDA's "*General Principles of Software Validation; Final Guidance for Industry and FDA Staff*." In accordance with the FDA guidance document "*Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, May 11, 2005*," documentation was provided that demonstrates the software changes performed as intended, met acceptance criteria, and did not have a negative impact on product performance, overall product safety, or patient safety.

The software for this device was determined to be a "moderate" level of concern, since a malfunction of, or a latent design flaw in the software device could lead to an erroneous diagnosis or a delay in delivery of appropriate medical care that would likely lead to minor injury. There was no change in the level of concern from the predicate iVue device.

Two clinical studies were performed to evaluate the repeatability and reproducibility and agreement to manual measurement of the iVue pachymetry scan for the corneal thickness (pachymetry), corneal epithelial thickness, and corneal stromal thickness mapping in normal subjects and corneal patients. Overall, the studies showed good repeatability and reproducibility for all study groups, all map zones, and for all 3 parameters evaluated and analyses demonstrating agreement of the automated corneal epithelial thickness segmentation.

Clinical Evaluation
Two clinical studies were conducted to demonstrate substantial equivalence:

1. ***Clinical Study for Repeatability and Reproducibility (R&R) of Corneal Epithelial Thickness Mapping with iVue SD-OCT***

   The objective of this clinical study was to evaluate the repeatability and reproducibility of the modified iVue software for the corneal thickness (pachymetry), the epithelial thickness, and the stromal thickness mapping using the ETM 6mm scan in normal subjects and corneal patients based on a crossed-study design and crossed random-effects ANOVA model.

   A heterogeneous population of qualified study subjects was evaluated and included a Normal Subjects group (12 subjects), a Corneal Patients group (47 subjects) further stratified into 4 subgroups: Contact Lens (12 subjects), Dry Eye (11 subjects), Post-Refractive Surgery (LRS) (12 subjects), and Keratoconus (KCN) (12 subjects). The study inclusion criteria required subjects who were 18 years of age or older, able to provide consent, and were

willing to complete the required examinations. In addition, subjects were qualified based on a history or clinical diagnosis of one or more of the following conditions:

- Dry eye patients with no history of refractive surgery
- Contact lens patients without complications, refractive surgery or dry eye
- Post-laser refractive surgery patients with 1 month post-surgery without complications
- Keratoconus patients with a clinical diagnosis of keratoconus in the study eye

The study exclusion criteria excluded those with the inability to complete the required SD-OCT scans (e.g., unable to fixate due to poor vision).

Three iVue devices were used. The same scanning protocol with device-specific designated operator was implemented to scan each qualified subject on 3 different devices, with 3 repeated epithelial thickness scans per device. Based on a crossed-study design, each study subject was imaged with all three iVue/operator pairs, and within each iVue/operator pair, at least three scans were acquired with the operator realigning the instrument on the study eye for each scan acquisition. To ensure realignment for each scan, the operator asked the test subject to sit back after a scan acquisition and then reposition for the next scan.

The evaluated ETM 6 mm scan showed good performance across all study groups in terms of ease of acquisition (no subjects excluded due to inability to perform the scan) and scan quality.

Seventy-one out of 598 total acquired scans (11.9%) were excluded from R&R analysis due to the following scan quality issues: decentration of the scan, eyelid artifacts, cropped OCT image, low SSI and motion artifacts. The percentage of disqualified scans was similar across Normal eyes (10.7%) and Corneal Patients eyes (12.1%). The distribution of non-qualifying scans across three different device/operator pairs was also similar: 20/194 (10.3%), 23/199 (11.6%) and 28/205 (13.6%) accordingly for iVue #24220, iVue #20847 and iVue #20779.

Out of 527 scans qualified for final analysis, 40 (7.6%) required manual edits of the segmentation lines. Manual edits were not required in Normal eyes scans, and ranged from 2.8% in Contact Lens sub-group to 17.9% in KCN sub-group, with similar distribution between the 3 iVue devices. For qualified scans, the operators reviewed the thickness maps for obvious segmentation error and reviewed the individual corneal meridian images to verify segmentation for erroneous maps. Segmentation edit tools were used to perform manual correction and then the epithelial map was reprocessed. Noticeable segmentation errors were manually corrected by the operator and marked for “Manual Correction” in the case report form. Scans with manual correction qualified for R&R data analysis.

A total of 59 subjects included in the data analysis had a demographic distribution by ethnicity that was majority Caucasian (40.7%), followed by Asian (25.4%), Hispanic (20.3%), African American (8.5%), and Other/Combined (5.1%). There was fair distribution of gender with 25 (42%) male and 34 (58%) female subjects enrolled.

Age distribution of Normal and Corneal Patient groups and subgroups is listed in table below. Age distribution was similar in Normal vs Corneal Patient group (total).

Age by Category	Min	Median	Mean	Max	SD
Normal	**18**	**43**	**42**	**63**	**15.7**
Corneal Patients (total)	**18**	**40**	**45**	**79**	**16.9**
Contact Lens Group	20	36	38	58	10.8
Dry Eye Group	30	62	57	79	18.8
Post Laser Refractive Surgery Group	30	47	50	78	18.7
Keratoconus Group	19	36	39	63	14.7

Age distribution for all subjects by enrollment Category.

Corneal Patients Study Group Characterization

Contact Lens Group	All subjects in the Contact Lens group wore soft contact lens regularly for 8 or more hours per day and for at least 3 months at the time of enrollment. The duration and the daily wear of contact lens are summarized below.

Contact lens wear data for the Contact Lens study group.

Contact Lens Wear	Min	Median	Mean	Max	SD
Duration (years)	2	11	11	20	6.3
Hours/Day	8	11	12	18	3.6

Dry Eye Group	For the Dry Eye group, the severity of the dry eye condition for each study subject was documented using Ocular Surface Disease Index (OSDI) score with a scale from 0 to 100 (mild to severe) and Tear Break Up Time (TBUT). The distribution of the OSDI score and TBUT for this group are summarized below.

OSDI Score and Tear Break Up Time (TBUT) distribution of the Dry Eye study group.

Dry Eye	Min	Median	Mean	Max	SD
ODSI Score	14.6	54.5	48.8	83.3	21.5
TBUT (seconds)	1	7	7	10	3

Post-LRS Group	For the Post LRS group, the majority (75%) had LASIK procedure versus the PRK procedure (25%), mainly for myopic vision correction (83.3%) and most had the procedure done at least 1 year or more prior to testing (91.7SD of 3.9108 scans%). The summary details are shown in Table below.

Clinical data for Post LRS study group

Procedure	**Total**	**% Total**
LASIK	9	75
PRK	3	25
Correction	**Total**	**% Total**
Myopic	10	83.3%
Hyperopic	1	8.3%
Astigmatism	1	8.3%
Duration since procedure		
> 1yr	11	91.7%
> 3mo	1	8.3%

KCN Group	The subjects in the KCN group all had clinical diagnosis of keratoconus. The clinical signs and severity of keratoconus for the study group are summarized in Table 7.5.4a and further details on corneal curvature are summarized in Table 7.5.4b. In addition to one subject had INTACS implant, we identified another subject in the KCN sub-group had PK (penetrating keratoplasty) five years prior to the study visit in the study eye. There were no other surgical treatments in the study eyes. (i.e., Cross linking)

KCN group distribution by clinical signs and severity

Clinical Signs	**Total**	**% Total**
Slit lamp exam	7	58.3%
Topographic patterns	11	91.7%
Slit lamp exam & Topographic patterns	6	50%
Retinoscope reflex	2	16.7%
Severity	**Total**	**% Total**
Mild	2	16.7%
Moderate	8	66.7%
Severe*	2	16.7%

Distribution of Steep K and Delta K (difference between Steep K and Flat K) in KCN group.

Corneal Curvature	**Min**	**Median**	**Mean**	**Max**	**SD**
Steep K	42.1	49	48.1	54	3.9
Delta K	0.6	2.3	2.4	4.3	1.1

Summary statistical parameters, including the mean, standard deviation (SD), range (minimum and maximum), Repeatability SD, Reproducibility SD, Reproducibility covariance (COV) and Reproducibility Limit for pachymetry, epithelial thickness and stromal thickness for Normal Patients, Corneal Patients, and Corneal Patient study subgroups is provided in the following tables. Repeatability standard deviation was similar to the Reproducibility standard deviation for all study parameters and therefore is not detailed separately in the summary tables below.

Pachymetry

Table 1a. Pachymetry measurements - Normal group

Normal Group (N scans=108)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Pachy	538.1	19.4	506.8	588.4	1.7	2.2	0.4%	6.0
T_2_5__Pachy	546.3	22.5	503.2	604.4	2.8	2.9	0.5%	8.0
ST_2_5__Pachy	564.0	23.2	528.4	628.5	3.7	3.9	0.7%	10.9
S_2_5__Pachy	577.3	22.4	542.1	642.6	4.4	4.7	0.8%	12.9
SN_2_5__Pachy	576.0	21.3	543.4	644.1	5.1	5.1	0.9%	14.2
N_2_5__Pachy	563.0	21.4	532.5	630.3	3.8	3.8	0.7%	10.6
IN_2_5__Pachy	551.6	20.2	520.0	607.0	2.3	2.7	0.5%	7.4
I_2_5__Pachy	544.1	19.7	506.4	592.5	2.1	2.7	0.5%	7.5
IT_2_5__Pachy	540.3	21.1	499.7	590.4	2.1	2.3	0.4%	6.4
T_5_6__Pachy	565.1	25.0	512.9	631.2	3.8	3.9	0.7%	10.7
ST_5_6__Pachy	593.4	24.8	553.7	667.6	5.6	5.8	1.0%	16.0
S_5_6__Pachy	613.9	23.8	573.7	685.3	6.3	6.8	1.1%	18.7
SN_5_6__Pachy	609.1	23.6	570.6	685.9	7.6	7.7	1.3%	21.3
N_5_6__Pachy	589.4	24.3	550.3	666.2	5.2	5.2	0.9%	14.5
IN_5_6__Pachy	573.4	22.9	538.4	635.3	3.7	3.7	0.7%	10.4
I_5_6__Pachy	564.7	22.1	523.2	621.0	3.3	3.5	0.6%	9.8
IT_5_6__Pachy	557.1	24.0	508.5	616.4	3.8	3.8	0.7%	10.6

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 1b. Pachymetry measurement – Corneal Patients pooled group

Corneal Patients Group (Pooled) (N scans=419)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Pachy	507.5	49.2	389.4	678.7	3.3	3.6	0.7%	10.0
T_2_5__Pachy	521.3	46.4	415.6	694.7	3.8	3.8	0.7%	10.6
ST_2_5__Pachy	541.2	46.6	439.5	717.9	4.7	4.8	0.9%	13.2
S_2_5__Pachy	554.3	47.2	445.1	726.2	5.3	5.4	1.0%	15.0
SN_2_5__Pachy	551.3	46.1	445.1	723.0	5.7	5.8	1.0%	16.0
N_2_5__Pachy	538.0	44.9	439.1	704.9	5.0	5.2	1.0%	14.4
IN_2_5__Pachy	524.7	46.3	430.3	687.3	4.2	4.5	0.9%	12.6
I_2_5__Pachy	513.3	50.7	404.7	679.6	3.3	3.7	0.7%	10.3
IT_2_5__Pachy	510.3	49.9	386.3	676.8	3.5	3.7	0.7%	10.2
T_5_6__Pachy	545.2	44.3	443.6	719.9	5.0	5.0	0.9%	14.0
ST_5_6__Pachy	575.1	46.8	461.1	747.7	6.7	6.8	1.2%	18.8
S_5_6__Pachy	595.6	48.7	478.4	757.8	8.6	8.8	1.5%	24.4
SN_5_6__Pachy	587.6	46.7	482.7	759.0	8.6	8.8	1.5%	24.4
N_5_6__Pachy	568.2	43.3	473.0	733.0	6.5	6.6	1.2%	18.2
IN_5_6__Pachy	553.3	42.9	460.6	711.2	5.2	5.5	1.0%	15.1
I_5_6__Pachy	540.4	47.7	444.2	707.9	5.6	5.8	1.1%	15.9
IT_5_6__Pachy	533.2	47.0	414.2	700.2	5.8	5.9	1.1%	16.3

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 1c. Pachymetry measurements – Contact Lens group

Contact Lens Group (N scans=108)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Pachy	513.4	40.0	425.5	589.0	1.6	2.1	0.4%	5.9
T_2_5__Pachy	522.7	40.5	432.1	597.9	2.5	2.8	0.5%	7.6
ST_2_5__Pachy	540.1	42.5	444.5	630.9	3.9	3.9	0.7%	10.7
S_2_5__Pachy	553.6	43.5	456.2	651.0	4.7	4.7	0.9%	13.1
SN_2_5__Pachy	551.4	42.1	455.4	641.8	4.7	4.7	0.8%	12.9
N_2_5__Pachy	538.3	40.3	449.3	620.2	3.7	3.7	0.7%	10.2
IN_2_5__Pachy	527.3	39.0	444.9	596.3	2.4	2.7	0.5%	7.6
I_2_5__Pachy	520.1	39.3	436.5	588.6	1.9	2.9	0.6%	7.9
IT_2_5__Pachy	516.8	39.5	430.4	586.0	1.9	2.7	0.5%	7.6
T_5_6__Pachy	541.4	41.7	443.6	618.7	3.7	3.7	0.7%	10.2
ST_5_6__Pachy	569.4	45.7	461.1	667.1	5.4	5.4	0.9%	14.9
S_5_6__Pachy	591.7	47.9	481.7	700.7	7.3	7.4	1.2%	20.4
SN_5_6__Pachy	585.9	44.7	483.5	688.2	7.6	7.8	1.3%	21.7
N_5_6__Pachy	565.3	41.3	473.6	652.9	5.1	5.1	0.9%	14.2
IN_5_6__Pachy	550.2	38.9	467.8	620.3	3.5	3.7	0.7%	10.2
I_5_6__Pachy	541.8	39.9	454.5	614.6	3.4	4.0	0.7%	11.0
IT_5_6__Pachy	534.1	40.5	442.4	610.3	3.5	4.1	0.8%	11.3

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 1d. Pachymetry measurements – Dry Eye group

Dry Eye Group (N scans=98)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Pachy	531.7	40.6	445.6	606.0	3.4	3.8	0.7%	10.5
T_2_5__Pachy	540.3	36.0	469.7	600.9	3.4	3.5	0.6%	9.6
ST_2_5__Pachy	558.3	38.7	485.4	640.9	5.2	5.2	0.9%	14.5
S_2_5__Pachy	573.3	40.2	502.9	673.7	6.8	7.0	1.2%	19.3
SN_2_5__Pachy	570.3	38.0	501.5	669.3	7.4	7.7	1.3%	21.3
N_2_5__Pachy	558.0	35.6	491.8	644.8	5.8	6.3	1.1%	17.4
IN_2_5__Pachy	548.9	34.2	485.9	613.0	4.1	4.8	0.9%	13.3
I_2_5__Pachy	538.0	41.4	436.0	590.4	3.7	4.0	0.7%	11.2
IT_2_5__Pachy	531.8	44.1	418.3	588.6	3.7	3.7	0.7%	10.3
T_5_6__Pachy	557.1	36.0	483.4	615.2	4.4	4.5	0.8%	12.4
ST_5_6__Pachy	588.9	38.8	518.4	681.9	8.8	8.8	1.5%	24.4
S_5_6__Pachy	616.6	42.0	550.0	736.3	13.1	13.4	2.2%	37.1
SN_5_6__Pachy	607.0	37.6	547.3	725.0	11.6	12.1	2.0%	33.4
N_5_6__Pachy	586.7	32.4	531.6	680.0	8.1	8.4	1.4%	23.3
IN_5_6__Pachy	575.0	29.9	522.1	634.0	5.1	5.5	1.0%	15.3
I_5_6__Pachy	559.7	42.4	453.6	615.1	5.1	5.2	0.9%	14.5
IT_5_6__Pachy	546.4	48.4	414.2	605.3	5.4	5.4	1.0%	14.9

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 1e. Pachymetry measurements – Post-LRS group

Post Laser Refractive Surgery Group (N scans=107)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Pachy	504.6	64.5	411.8	678.7	1.5	1.9	0.4%	5.2
T_2_5__Pachy	521.3	60.9	435.5	694.7	3.2	3.4	0.6%	9.3
ST_2_5__Pachy	538.6	63.4	439.5	717.9	4.2	4.2	0.8%	11.7
S_2_5__Pachy	552.0	63.2	445.1	726.2	4.5	4.5	0.8%	12.5
SN_2_5__Pachy	548.0	63.1	445.1	723.0	4.9	4.9	0.9%	13.7
N_2_5__Pachy	534.9	61.6	439.1	704.9	4.3	4.4	0.8%	12.3
IN_2_5__Pachy	527.0	59.9	432.0	687.3	3.4	3.9	0.7%	10.8
I_2_5__Pachy	522.0	58.2	433.8	679.6	3.0	3.5	0.7%	9.7
IT_2_5__Pachy	516.8	57.8	433.7	676.8	2.9	3.2	0.6%	8.8
T_5_6__Pachy	548.5	58.9	464.0	719.9	4.9	5.2	0.9%	14.3
ST_5_6__Pachy	577.0	60.7	472.5	747.7	5.7	5.9	1.0%	16.2
S_5_6__Pachy	599.0	57.7	484.3	757.8	6.3	6.4	1.1%	17.7
SN_5_6__Pachy	590.8	58.7	486.1	759.0	7.3	7.3	1.2%	20.3
N_5_6__Pachy	569.1	58.1	473.0	733.0	6.4	6.4	1.1%	17.7
IN_5_6__Pachy	558.4	56.2	460.6	711.2	5.6	5.8	1.0%	16.2
I_5_6__Pachy	553.2	54.3	465.6	707.9	4.6	4.9	0.9%	13.7
IT_5_6__Pachy	543.0	54.1	463.1	700.2	4.7	5.0	0.9%	13.7

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 1f Pachymetry measurements - KCN group

Keratoconus Group (N scans=106)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Pachy	482.1	32.5	389.4	522.2	5.4	5.5	1.1%	15.1
T_2_5__Pachy	502.1	35.4	415.6	544.6	5.3	5.3	1.1%	14.6
ST_2_5__Pachy	529.1	30.6	450.5	567.3	5.5	5.6	1.1%	15.5
S_2_5__Pachy	539.9	29.3	463.3	576.5	4.9	5.0	0.9%	14.0
SN_2_5__Pachy	536.8	27.3	463.6	570.0	5.3	5.5	1.0%	15.2
N_2_5__Pachy	522.3	27.3	453.1	563.5	6.0	6.1	1.2%	16.9
IN_2_5__Pachy	497.2	31.1	430.3	548.0	5.9	6.1	1.2%	16.9
I_2_5__Pachy	474.7	38.1	404.7	533.3	4.2	4.4	0.9%	12.2
IT_2_5__Pachy	477.2	38.9	386.3	532.5	4.8	4.8	1.0%	13.3
T_5_6__Pachy	534.6	32.8	461.1	574.7	6.3	6.5	1.2%	17.9
ST_5_6__Pachy	566.3	34.6	478.6	608.7	6.4	6.7	1.2%	18.6
S_5_6__Pachy	576.6	36.2	478.4	623.3	6.6	6.6	1.2%	18.4
SN_5_6__Pachy	568.4	33.8	482.7	616.7	7.3	7.6	1.3%	21.0
N_5_6__Pachy	553.3	28.4	480.2	588.6	6.0	6.1	1.1%	17.0
IN_5_6__Pachy	531.2	28.1	472.5	579.0	6.3	6.5	1.2%	17.9
I_5_6__Pachy	508.2	34.9	444.2	558.9	8.1	8.1	1.6%	22.4
IT_5_6__Pachy	510.3	34.6	431.5	568.4	8.3	8.3	1.6%	23.1

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Epithelial Thickness

Table 2a. Epithelial thickness measurements - Normal group.

Normal Group (N scans=108)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Epi	52.9	3.4	47.5	61.2	0.9	0.9	1.8%	2.6
T_2_5__Epi	52.2	3.3	45.9	61.2	1.2	1.2	2.3%	3.4
ST_2_5__Epi	51.7	2.8	47.1	59.8	1.3	1.3	2.5%	3.5
S_2_5__Epi	52.0	2.8	47.3	59.9	1.2	1.2	2.4%	3.4
SN_2_5__Epi	52.9	3.1	47.6	61.5	1.2	1.2	2.2%	3.3
N_2_5__Epi	53.4	3.0	47.3	60.7	1.1	1.1	2.0%	3.0
IN_2_5__Epi	53.7	3.6	47.8	61.2	0.9	0.9	1.6%	2.4
I_2_5__Epi	54.0	3.9	47.7	65.3	1.0	1.0	1.8%	2.8
IT_2_5__Epi	53.2	3.9	46.4	63.4	1.1	1.1	2.1%	3.1
T_5_6__Epi	52.2	3.2	45.2	59.8	1.3	1.3	2.5%	3.6
ST_5_6__Epi	50.8	2.6	44.8	60.1	1.4	1.5	2.9%	4.0
S_5_6__Epi	50.9	3.0	43.7	60.7	1.3	1.4	2.7%	3.8
SN_5_6__Epi	53.0	3.4	46.9	62.9	1.2	1.2	2.3%	3.4
N_5_6__Epi	53.6	2.8	48.1	60.8	1.1	1.1	2.0%	3.0
IN_5_6__Epi	53.8	3.3	48.1	59.8	1.0	1.0	1.8%	2.7
I_5_6__Epi	54.1	3.8	47.9	66.0	1.3	1.3	2.3%	3.5
IT_5_6__Epi	53.4	3.6	46.7	62.4	1.3	1.3	2.4%	3.6

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 2b. Epithelial thickness measurements – Corneal Patients pooled group

Corneal Patients Group (Pooled) (N scans=419)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Epi	51.3	4.6	38.2	64.1	1.2	1.2	2.4%	3.4
T_2_5__Epi	51.3	4.7	39.7	65.2	1.4	1.4	2.7%	3.9
ST_2_5__Epi	51.7	4.4	40.6	63.1	1.3	1.4	2.7%	3.8
S_2_5__Epi	51.8	4.6	39.1	63.7	1.4	1.4	2.7%	3.8
SN_2_5__Epi	52.5	4.5	41.8	63.5	1.5	1.5	2.8%	4.1
N_2_5__Epi	53.1	4.2	43.1	69.1	1.4	1.4	2.6%	3.9
IN_2_5__Epi	52.9	4.1	41.8	65.6	1.4	1.4	2.6%	3.8
I_2_5__Epi	52.2	4.9	38.0	64.9	1.4	1.4	2.7%	3.9
IT_2_5__Epi	51.4	5.4	37.2	65.8	1.4	1.4	2.7%	3.9
T_5_6__Epi	51.7	4.5	40.6	65.2	1.6	1.7	3.2%	4.6
ST_5_6__Epi	51.5	4.7	37.9	64.5	1.7	1.7	3.4%	4.8
S_5_6__Epi	51.1	4.8	36.5	65.1	1.7	1.7	3.4%	4.8
SN_5_6__Epi	52.3	4.6	41.1	66.1	1.6	1.7	3.2%	4.6
N_5_6__Epi	53.4	4.6	39.2	72.8	1.6	1.7	3.1%	4.7
IN_5_6__Epi	53.7	4.3	41.5	65.9	1.5	1.6	2.9%	4.3
I_5_6__Epi	53.0	4.4	39.1	66.7	1.9	1.9	3.6%	5.3
IT_5_6__Epi	52.4	4.7	40.9	72.5	1.9	1.9	3.6%	5.3

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 2c. Epithelial thickness measurements – Contact Lens group

Contact Lens Group (N scans=108)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Epi	51.0	3.6	43.2	57.8	0.8	0.9	1.8%	2.6
T_2_5__Epi	50.6	3.4	42.3	56.9	0.9	1.1	2.1%	3.0
ST_2_5__Epi	50.9	3.4	43.7	57.2	1.0	1.1	2.2%	3.0
S_2_5__Epi	51.4	3.4	45.3	57.1	1.1	1.1	2.2%	3.2
SN_2_5__Epi	52.0	3.2	46.1	57.9	1.1	1.2	2.3%	3.2
N_2_5__Epi	51.9	2.9	45.6	57.6	0.9	1.0	2.0%	2.9
IN_2_5__Epi	52.0	2.9	45.4	57.0	0.8	0.8	1.6%	2.3
I_2_5__Epi	52.1	3.2	45.2	58.4	0.8	0.9	1.7%	2.5
IT_2_5__Epi	51.0	3.2	43.8	57.3	0.8	0.9	1.8%	2.6
T_5_6__Epi	50.8	2.9	43.3	55.4	1.1	1.3	2.6%	3.7
ST_5_6__Epi	51.0	3.3	44.5	57.8	1.6	1.7	3.3%	4.7
S_5_6__Epi	51.2	3.4	44.5	57.4	1.6	1.7	3.3%	4.6
SN_5_6__Epi	52.5	3.4	46.0	59.3	1.3	1.4	2.7%	3.9
N_5_6__Epi	52.5	3.2	46.8	60.3	1.1	1.3	2.4%	3.5
IN_5_6__Epi	52.7	3.1	47.2	60.4	0.9	1.0	1.9%	2.7
I_5_6__Epi	52.7	3.3	46.8	58.9	1.0	1.1	2.1%	3.0
IT_5_6__Epi	51.6	3.2	44.4	57.7	0.9	1.1	2.0%	2.9

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 2d. Epithelial thickness measurements – Dry Eye group

Dry Eye Group (N scans=98)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Epi	51.7	3.4	43.6	60.0	1.6	1.6	3.2%	4.6
T_2_5__Epi	50.5	3.3	42.7	58.6	1.9	1.9	3.9%	5.4
ST_2_5__Epi	49.9	4.3	40.6	59.8	1.8	1.8	3.6%	5.0
S_2_5__Epi	50.0	5.5	39.1	63.7	2.0	2.0	4.1%	5.7
SN_2_5__Epi	51.1	5.2	41.8	63.5	2.4	2.4	4.7%	6.7
N_2_5__Epi	52.1	4.7	43.7	69.1	2.1	2.2	4.3%	6.1
IN_2_5__Epi	52.6	4.6	41.8	65.6	2.2	2.2	4.2%	6.1
I_2_5__Epi	52.7	4.4	40.9	64.9	2.4	2.4	4.5%	6.5
IT_2_5__Epi	52.1	4.0	42.2	65.3	2.2	2.2	4.1%	6.0
T_5_6__Epi	50.2	4.2	42.9	64.6	2.0	2.1	4.1%	5.8
ST_5_6__Epi	49.1	5.2	37.9	60.1	1.9	2.0	4.1%	5.5
S_5_6__Epi	49.3	6.9	36.5	65.1	2.0	2.1	4.2%	5.8
SN_5_6__Epi	50.9	6.3	41.1	66.1	2.4	2.4	4.7%	6.6
N_5_6__Epi	52.8	6.4	43.7	72.8	2.5	2.5	4.8%	7.0
IN_5_6__Epi	52.5	5.0	41.5	65.7	2.5	2.5	4.7%	6.8
I_5_6__Epi	52.4	5.1	39.1	66.7	2.9	2.9	5.5%	8.0
IT_5_6__Epi	52.4	5.4	41.7	72.5	2.6	2.6	4.9%	7.2

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 2e. Epithelial thickness measurements – Post-LRS group

Post Laser Refractive Surgery Group (N scans=107)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Epi	54.0	4.6	42.8	64.1	0.6	0.7	1.2%	1.9
T_2_5__Epi	54.1	4.7	43.6	65.2	1.0	1.1	2.0%	3.0
ST_2_5__Epi	53.2	4.4	45.2	63.1	0.9	1.0	1.8%	2.7
S_2_5__Epi	52.9	4.5	44.1	62.2	0.8	0.8	1.5%	2.2
SN_2_5__Epi	53.4	4.1	45.6	61.4	0.7	0.7	1.4%	2.1
N_2_5__Epi	54.4	3.8	47.0	62.2	0.7	0.8	1.5%	2.3
IN_2_5__Epi	55.2	3.7	48.1	62.8	0.8	0.8	1.5%	2.4
I_2_5__Epi	56.1	3.7	47.3	63.3	0.8	0.9	1.5%	2.4
IT_2_5__Epi	55.5	4.8	44.5	65.8	0.9	1.0	1.7%	2.7
T_5_6__Epi	52.4	4.2	41.4	62.1	1.4	1.5	3.0%	4.3
ST_5_6__Epi	51.4	3.6	42.4	59.2	1.4	1.6	3.1%	4.3
S_5_6__Epi	51.5	3.7	42.7	58.0	1.1	1.2	2.3%	3.3
SN_5_6__Epi	53.0	3.8	43.5	58.3	1.0	1.1	2.0%	3.0
N_5_6__Epi	54.0	3.2	46.1	59.9	1.1	1.1	2.1%	3.1
IN_5_6__Epi	54.7	3.8	46.6	62.4	1.1	1.2	2.2%	3.3
I_5_6__Epi	54.9	3.9	45.2	63.2	1.4	1.6	2.9%	4.4
IT_5_6__Epi	54.6	4.2	40.9	65.5	1.4	1.6	2.9%	4.4

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 2f. Epithelial thickness measurements – KCN group

Keratoconus Group (N scans=106)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Epi	48.6	4.8	38.2	58.4	1.4	1.5	3.0%	4.1
T_2_5__Epi	49.8	5.6	39.7	61.1	1.3	1.4	2.7%	3.8
ST_2_5__Epi	52.6	4.4	44.3	61.7	1.5	1.5	2.9%	4.3
S_2_5__Epi	52.7	4.5	45.1	61.8	1.3	1.3	2.4%	3.6
SN_2_5__Epi	53.3	5.0	44.2	62.2	1.2	1.2	2.3%	3.5
N_2_5__Epi	53.9	4.9	43.1	61.7	1.2	1.3	2.3%	3.5
IN_2_5__Epi	51.8	4.2	43.9	63.2	1.3	1.3	2.5%	3.6
I_2_5__Epi	48.1	4.6	38.0	55.8	1.1	1.2	2.4%	3.2
IT_2_5__Epi	47.0	5.5	37.2	58.4	1.2	1.3	2.7%	3.5
T_5_6__Epi	53.4	5.7	40.6	65.2	1.7	1.7	3.2%	4.7
ST_5_6__Epi	54.3	4.9	43.7	64.5	1.6	1.7	3.1%	4.7
S_5_6__Epi	52.1	4.4	42.1	60.8	1.8	1.9	3.6%	5.2
SN_5_6__Epi	52.7	4.5	41.2	63.8	1.5	1.6	3.1%	4.5
N_5_6__Epi	54.4	4.7	39.2	62.7	1.4	1.6	3.0%	4.4
IN_5_6__Epi	54.7	4.7	46.2	65.9	1.1	1.2	2.2%	3.4
I_5_6__Epi	51.8	4.6	42.5	61.2	1.7	1.7	3.2%	4.6
IT_5_6__Epi	51.1	5.1	42.7	62.4	2.1	2.1	4.1%	5.8

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Stromal Thickness

Table 3a. Stromal thickness measurements - Normal group

Normal Group (N scans=108)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Stroma	485.2	20.0	449.8	539.5	1.6	2.0	0.4%	5.4
T_2_5__Stroma	494.1	23.1	450.8	555.7	2.4	2.6	0.5%	7.1
ST_2_5__Stroma	512.4	23.6	475.9	579.1	3.4	3.7	0.7%	10.3
S_2_5__Stroma	525.3	22.9	490.9	594.1	4.2	4.6	0.9%	12.7
SN_2_5__Stroma	523.2	21.9	491.2	593.8	4.9	4.9	0.9%	13.7
N_2_5__Stroma	509.6	21.8	476.7	578.9	3.6	3.6	0.7%	10.0
IN_2_5__Stroma	497.9	20.5	463.8	556.7	2.1	2.5	0.5%	7.0
I_2_5__Stroma	490.1	20.1	450.4	542.5	1.9	2.5	0.5%	6.9
IT_2_5__Stroma	487.2	21.7	444.3	540.9	1.9	2.1	0.4%	5.8
T_5_6__Stroma	512.9	25.4	461.2	581.9	3.6	3.7	0.7%	10.2
ST_5_6__Stroma	542.6	25.0	503.9	618.6	5.4	5.7	1.0%	15.7
S_5_6__Stroma	563.0	24.1	524.2	634.2	6.2	6.7	1.2%	18.5
SN_5_6__Stroma	556.0	24.2	519.8	634.5	7.6	7.6	1.4%	21.1
N_5_6__Stroma	535.7	24.5	498.2	614.0	5.1	5.1	0.9%	14.1
IN_5_6__Stroma	519.6	23.0	482.6	583.7	3.4	3.5	0.7%	9.7
I_5_6__Stroma	510.5	22.4	468.4	570.4	3.2	3.3	0.7%	9.3
IT_5_6__Stroma	503.7	24.3	451.0	567.0	3.6	3.6	0.7%	10.1

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 3b. Stromal thickness measurements – Corneal Patients pooled group

Corneal Patients Group (Pooled) (N scans=419)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Stroma	456.2	49.7	351.2	630.5	2.8	3.1	0.7%	8.5
T_2_5__Stroma	470.0	46.8	375.9	646.2	3.5	3.6	0.8%	9.9
ST_2_5__Stroma	489.5	48.2	387.3	671.9	4.7	4.8	1.0%	13.3
S_2_5__Stroma	502.5	49.2	392.3	682.1	5.3	5.4	1.1%	14.9
SN_2_5__Stroma	498.8	48.0	391.2	677.4	5.6	5.6	1.1%	15.6
N_2_5__Stroma	484.9	46.7	383.3	656.9	4.7	4.8	1.0%	13.4
IN_2_5__Stroma	471.8	47.3	372.6	637.9	3.8	4.1	0.9%	11.3
I_2_5__Stroma	461.0	50.2	361.5	628.1	3.0	3.3	0.7%	9.1
IT_2_5__Stroma	458.9	49.5	349.1	627.4	3.2	3.3	0.7%	9.1
T_5_6__Stroma	493.4	45.2	389.7	672.0	4.8	5.0	1.0%	13.9
ST_5_6__Stroma	523.6	48.5	407.4	703.4	6.8	7.0	1.3%	19.3
S_5_6__Stroma	544.5	50.9	425.5	715.1	8.8	9.0	1.7%	25.0
SN_5_6__Stroma	535.3	48.4	425.4	714.4	8.6	8.9	1.7%	24.6
N_5_6__Stroma	514.8	45.0	415.0	686.6	6.4	6.4	1.2%	17.8
IN_5_6__Stroma	499.6	44.5	400.3	662.5	5.2	5.3	1.1%	14.8
I_5_6__Stroma	487.5	47.9	397.3	653.5	5.4	5.5	1.1%	15.3
IT_5_6__Stroma	480.8	47.5	355.8	649.5	5.2	5.3	1.1%	14.7

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 3c. Stromal thickness measurements – Contact Lens group

Contact Lens Group (N scans=108)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Stroma	462.5	38.8	373.9	532.5	1.4	1.8	0.4%	4.9
T_2_5__Stroma	472.1	39.6	378.6	542.3	2.2	2.4	0.5%	6.6
ST_2_5__Stroma	489.2	41.8	391.1	573.8	3.5	3.6	0.7%	9.9
S_2_5__Stroma	502.1	43.3	400.6	594.0	4.4	4.4	0.9%	12.3
SN_2_5__Stroma	499.5	42.2	399.9	586.7	4.3	4.4	0.9%	12.2
N_2_5__Stroma	486.4	40.2	394.2	565.8	3.5	3.5	0.7%	9.7
IN_2_5__Stroma	475.3	38.6	389.9	541.1	2.3	2.6	0.5%	7.1
I_2_5__Stroma	468.0	38.4	382.4	531.7	1.9	2.6	0.6%	7.3
IT_2_5__Stroma	465.8	38.5	376.6	530.5	1.8	2.5	0.5%	7.0
T_5_6__Stroma	490.6	41.3	389.7	563.9	3.3	3.4	0.7%	9.3
ST_5_6__Stroma	518.4	45.2	407.4	610.2	5.3	5.3	1.0%	14.8
S_5_6__Stroma	540.6	47.7	427.3	645.4	7.1	7.4	1.4%	20.5
SN_5_6__Stroma	533.4	45.3	425.4	633.3	7.4	7.9	1.5%	21.8
N_5_6__Stroma	512.8	41.9	415.0	598.5	4.8	5.1	1.0%	14.1
IN_5_6__Stroma	497.5	39.3	409.1	565.4	3.5	3.6	0.7%	10.0
I_5_6__Stroma	489.1	39.9	397.5	558.7	3.4	3.8	0.8%	10.6
IT_5_6__Stroma	482.5	40.2	385.9	555.4	3.3	3.8	0.8%	10.4

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 3d. Stromal thickness measurements – Dry Eye group

Dry Eye Group (N scans=98)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Stroma	480.0	42.2	390.9	560.3	3.0	3.4	0.7%	9.5
T_2_5__Stroma	489.8	37.9	414.6	555.2	3.2	3.2	0.7%	9.0
ST_2_5__Stroma	508.4	41.4	430.4	600.3	5.2	5.2	1.0%	14.4
S_2_5__Stroma	523.3	43.5	448.1	633.4	6.8	6.9	1.3%	19.0
SN_2_5__Stroma	519.2	40.9	449.0	627.5	7.2	7.4	1.4%	20.4
N_2_5__Stroma	506.0	38.5	433.2	597.7	5.4	5.8	1.1%	16.1
IN_2_5__Stroma	496.4	37.0	425.1	565.9	3.5	4.3	0.9%	11.8
I_2_5__Stroma	485.4	43.8	378.5	543.4	3.0	3.3	0.7%	9.1
IT_2_5__Stroma	479.7	46.7	358.3	540.0	3.1	3.1	0.7%	8.7
T_5_6__Stroma	506.9	38.7	426.7	569.0	4.2	4.2	0.8%	11.7
ST_5_6__Stroma	539.8	42.2	460.8	641.6	8.6	8.6	1.6%	23.8
S_5_6__Stroma	567.3	46.5	496.5	697.5	13.4	13.7	2.4%	38.0
SN_5_6__Stroma	556.1	41.1	493.4	683.9	11.5	11.9	2.1%	33.0
N_5_6__Stroma	533.9	35.5	470.6	632.4	7.6	7.8	1.5%	21.5
IN_5_6__Stroma	522.5	32.7	470.2	586.0	4.9	5.2	1.0%	14.5
I_5_6__Stroma	507.3	45.1	398.2	569.7	5.0	5.1	1.0%	14.0
IT_5_6__Stroma	494.0	52.3	355.8	557.8	5.1	5.1	1.0%	14.1

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 3e. Stromal thickness measurements – Post-LRS group

Post Laser Refractive Surgery Group (N scans=107)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Stroma	450.6	66.9	355.5	630.5	1.5	1.8	0.4%	5.0
T_2_5__Stroma	467.2	63.0	380.3	646.2	3.5	3.7	0.8%	10.4
ST_2_5__Stroma	485.4	65.5	387.3	671.9	4.1	4.2	0.9%	11.7
S_2_5__Stroma	499.1	65.5	392.3	682.1	4.9	4.9	1.0%	13.6
SN_2_5__Stroma	494.6	65.1	391.2	677.4	5.0	5.0	1.0%	13.9
N_2_5__Stroma	480.5	63.4	383.3	656.9	3.9	4.0	0.8%	11.2
IN_2_5__Stroma	471.8	61.9	372.6	637.9	3.3	3.7	0.8%	10.2
I_2_5__Stroma	465.9	60.1	372.4	628.1	2.9	3.3	0.7%	9.3
IT_2_5__Stroma	461.3	60.1	373.6	627.4	3.0	3.2	0.7%	8.8
T_5_6__Stroma	496.1	59.4	415.2	672.0	5.5	5.9	1.2%	16.4
ST_5_6__Stroma	525.6	62.1	422.0	703.4	6.4	6.6	1.3%	18.4
S_5_6__Stroma	547.5	60.1	428.1	715.1	6.6	6.7	1.2%	18.5
SN_5_6__Stroma	537.7	60.2	431.3	714.4	7.5	7.5	1.4%	20.7
N_5_6__Stroma	515.1	59.4	418.1	686.6	6.8	6.8	1.3%	18.9
IN_5_6__Stroma	503.7	58.2	400.3	662.5	6.0	6.2	1.2%	17.2
I_5_6__Stroma	498.4	55.1	402.8	653.5	5.0	5.4	1.1%	14.9
IT_5_6__Stroma	488.4	55.2	404.7	649.5	4.8	5.1	1.0%	14.2

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Table 3f. Stromal thickness measurements – KCN group

Keratoconus Group (N scans=106)								
	Mean	SD	Min	Max	Repeatability	Reproducibility		
					SD	SD	COV	Limit*
Zonal Parameters								
C_2__Stroma	433.5	31.6	351.2	471.9	4.4	4.4	1.0%	12.3
T_2_5__Stroma	452.4	33.4	375.9	486.6	4.5	4.6	1.0%	12.7
ST_2_5__Stroma	476.5	32.2	398.4	520.0	5.6	5.7	1.2%	15.8
S_2_5__Stroma	487.2	31.7	406.8	530.1	5.0	5.1	1.1%	14.2
SN_2_5__Stroma	483.5	29.9	404.3	521.7	5.3	5.4	1.1%	15.1
N_2_5__Stroma	468.4	29.8	395.4	513.0	5.4	5.5	1.2%	15.4
IN_2_5__Stroma	445.4	31.1	378.9	498.5	5.2	5.4	1.2%	15.0
I_2_5__Stroma	426.6	35.6	361.5	479.8	3.7	3.8	0.9%	10.6
IT_2_5__Stroma	430.2	35.7	349.1	477.4	4.1	4.1	1.0%	11.5
T_5_6__Stroma	481.2	33.1	406.4	521.2	5.8	6.0	1.2%	16.6
ST_5_6__Stroma	512.0	36.4	423.1	563.9	6.7	7.1	1.4%	19.8
S_5_6__Stroma	524.5	37.8	425.5	576.4	6.7	6.9	1.3%	19.0
SN_5_6__Stroma	515.7	34.5	426.8	565.0	7.3	7.8	1.5%	21.7
N_5_6__Stroma	498.9	30.7	421.8	533.4	5.7	5.9	1.2%	16.5
IN_5_6__Stroma	476.5	28.9	411.9	523.7	5.8	5.9	1.2%	16.5
I_5_6__Stroma	456.4	33.1	397.3	503.5	7.3	7.3	1.6%	20.1
IT_5_6__Stroma	459.2	32.4	386.4	511.7	6.9	6.9	1.5%	19.1

* Reproducibility Limit is the 95% limit for the difference between measurements under the reproducibility conditions. Reproducibility Limit = 2.8 x Reproducibility SD per ISO 5725-1 and ISO 5725-6.

Summary

Overall, the study showed good repeatability and reproducibility for all study groups, all map zones, and for all 3 parameters evaluated – corneal pachymetry, corneal epithelial, and corneal stromal thickness.

2. *Clinical Study for Agreement of Corneal Epithelial Thickness Mapping with iVue SD-OCT to Manual Measurement*

The objective of this clinical study was to evaluate the agreement to manual measurement of the iVue with modified software with the participation of 3 study sites, each with one iVue instrument for the OCT data collection. The agreement to manual measurement of the software was evaluated based on the agreement between the software output and the manual measurements by 3 qualified graders. The manual measurements were performed with a 2-section caliper tool that was available in the previously cleared iVue software.

The agreement was assessed based on the combined group of 87 study eyes of 87 subjects, consisting of 17 normal subjects, 16 contact lens normal subjects, 18 dry eye subjects, 20 post-laser refractive surgery subjects, and 16 keratoconus subjects. No patients in the agreement study keratoconus subgroup had prior surgery.

The iVue scan was easy to acquire. Of the 88 subjects met the enrollment criteria, only one dry eye subject was disqualified due to poor image quality. Good image quality was obtained in 75 of the 88 subjects on the first scan and therefore didn't require additional scans, another 12 subjects required 1 or 2 additional scans to yield a good quality image, and only one subject was excluded due to poor image quality.

The automatic segmentation algorithm worked well in 78 scans (90%) out of 87 total study scans and no manual editing was performed for these scans. For the 9 scans which required manual editing, 5 were from the keratoconus sub-group.

The ethnic distribution was largely Caucasian (48.9%), followed by Asian and Hispanic at 23.9% and 15.9% respectively. Majority of the subjects enrolled in the study were female. The study eyes consisted of 44 right eyes and 44 left eyes from the 88 qualified subjects.

Age distribution of the combined group and each sub-group are provided in the table below, covering a wide age range.

Age Distribution	Min	Median	Mean	Max	SD
Entire Group	**23**	**34**	**38.6**	**73**	**12.6**
Normal	25	32	33.5	66	10.4
Contact Lens	25	30	35.2	58	11.1
Dry Eye	24	51	46.5	73	15.3
Post Laser Refractive Surgery	23	38	38.8	56	8.9
Keratoconus	25	34	38.0	62	11.7

Table: Age distribution by entire study group and by sub-groups.

Of the 16 subjects in the Contact Lens sub-group, 15 subjects wore soft contact lens and 1 subject wore hard contact lens. All subjects wore contact lens regularly for 8 or more hours per day and for at least one year at the time of enrollment. The duration and the daily wear of contact lens are summarized in table below.

Contact Lens Wear	Min	Median	Mean	Max	SD
Duration (yr)	1	10	11	20	6.07
Hours/Day	8	12	12.6	16	2.06

Table: Contact lens wear data for the Contact Lens sub-group.

For the 18 subjects in the Dry Eye group, the severity of the dry eye condition for each study subject was documented using Ocular Surface Disease Index (OSDI) score with a scale from 0 to 100 (mild to severe) and Tear Break Up Time (TBUT). The distribution of the OSDI score and TBUT for the dry eye subjects are summarized in table below.

Dry Eye	Min	Median	Mean	Max	SD
OSDI score	6.3	20.8	22.2	40.9	5.28
TBUT	1	4.8	4.6	7	1.83

Table: OSDI Score and Tear Break Up Time (TBUT) distribution of the Dry Eye sub-group.

For the 20 subjects in the Post LRS group, the majority (75%) had LASIK procedure versus the PRK procedure (25%), mainly for myopic vision correction (83.3%) and most had the procedure done at least 1 year or more prior to testing (83.3%). The summary details are shown in the table below.

Procedure	Total	% Total (n=20)
LASIK	15	75.0%
PRK	5	25.0%
Correction		
Myopic	13	65.0%
Hyperopic	4	20.0%
Astigmatism	0	0.0%
Mixed*	3	15.0%
Duration since procedure		
> 1yr	16	80.0%
> 3mo	4	20.0%
> 1mo	0	0.0%

Table: Summary of the Post LRS sub-group. *Mixed represented procedures either combining myopic correction with astigmatism correction or hyperopic correction with astigmatism correction.

The 16 subjects in the KCN sub-group all had clinical diagnosis of keratoconus. The clinical signs are provided in Table a, severity of keratoconus for the KCN subjects are summarized in Table b, and details on corneal curvature are summarized in Table c.

Subject ID	Severity	slit lamp thinning	slit lamp protrusion	slit lamp munson	slit lamp vogt	slit lamp fleisher	slit lamp rizutti	topo bow-tie	topo steep	topo claw
DS-10	moderate	1								1
DS-12	mild	1								1
DS-21	moderate	1			1				1	
DS-29	moderate	1	1						1	1
DS-31	severe	1							1	1
DS-32	moderate	1							1	1
DS-34	severe	1	1						1	
DS-36	moderate	1						1	1	
DS-37	mild	1							1	
MP-08	severe								1	
MP-14	moderate							1	1	
MP-19	moderate	1	1							
MP-25	mild								1	
MP-28	severe									1
MP-31	moderate							1		
K1, SH	moderate									1

Table a. KCN subjects diagnosis by clinical signs.

Severity	**Total**	**% Total (n=16)**
Mild	3	18.8%
Moderate	9	56.3%
Severe	4	25.0%

Table b. KCN group distribution by severity

Corneal Curvature	Min	Median	Mean	Max	SD
Steep K	41.80	47.76	49.65	70.80	6.47
Delta K	0.36	2.67	3.30	8.33	2.17

Table c. Distribution of Steep K and Delta K (difference between Steep K and Flat K) of the KCN sub-group.

As summarized in Table 4A, the mean of differences between the software output and the manual measurements for all zonal parameters is less than 0.7 µm (<1.3% of average epithelial thickness of 54 µm) for corneal epithelial mapping, less than 1.9 µm (<0.4% of average stroma thickness of 490 µm) for corneal stroma mapping, and less than 2.3 µm (<0.4% of average corneal thickness of 543 µm) for pachymetry mapping. The overall difference between the software output and the manual measurements is negligible.

Table 4A. Summary of the mean of differences by measurement zone and by corneal map type.

Mean of Differences (µm) (N = 87)	Epithelial			Stroma			Pachymetry		
	2 mm zone	2 to 5 mm zone	5 to 6 mm zone	2 mm zone	2 to 5 mm zone	5 to 6 mm zone	2 mm zone	2 to 5 mm zone	5 to 6 mm zone
mean	-0.4	0.2	0.4	-1.2	0.5	0.3	-1.6	0.7	0.7
min		-0.1	-0.3		-0.8	-0.2		-0.6	-0.2
max		0.3	0.7		1.9	1.2		2.3	1.3

As summarized in Tables 4B and 4C, the limits of agreement between the software output and the manual measurements for all zonal parameters are within the range of (-6.2 ~ 5.9) µm for corneal epithelial mapping, within the range of (-9.7 ~ 10.4) µm for corneal stroma mapping, and within the range of (-7.9 ~ 9.6) µm for pachymetry mapping, indicating good agreement between the 2 methods.

Table 4B. Summary of the LOA lower bound by measurement zone and by corneal map type.

LOA Lower Bound (µm) (N = 87)	Epithelial			Stroma			Pachymetry		
	2 mm zone	2 to 5 mm zone	5 to 6 mm zone	2 mm zone	2 to 5 mm zone	5 to 6 mm zone	2 mm zone	2 to 5 mm zone	5 to 6 mm zone
mean	-3.4	-4.0	-4.8	-4.7	-4.4	-7.2	-3.5	-3.0	-4.5
min		-4.4	-6.2		-5.7	-9.7		-4.5	-7.9
max		-3.7	-4.3		-3.6	-5.5		-2.2	-2.0

Table 4C. Summary of the LOA upper bound by measurement zone and by corneal map type.

LOA Upper Bound (µm) (N = 87 subjects)	Epithelial			Stroma			Pachymetry		
	2 mm zone	2 to 5 mm zone	5 to 6 mm zone	2 mm zone	2 to 5 mm zone	5 to 6 mm zone	2 mm zone	2 to 5 mm zone	5 to 6 mm zone
mean	2.6	4.4	5.6	2.4	5.5	7.9	0.3	4.5	5.9
min		4.1	5.2		3.5	5.7		2.5	3.8
max		4.7	5.9		7.5	10.4		6.7	9.6

In summary, the study demonstrated good agreement between the iVue with modified software and the manual measurements.

Limits of Agreement

The limits of agreement of the corneal thickness mapping between the software output and manual measurements are provided for the Combined Group, and, for additional information, also for the 5 sub-groups (Normal, Contact Lens, Dry Eye, Post-LRS, and KCN) respectively.

The Bland-Altman plots for the agreement between software output and manual measurement are provided for the Combined Group and the 5 sub-groups. The Bland-Altman plot is a scatter plot of the difference between the software-based and manual methods, using manual measurements as reference as represented by the horizontal axis. Reference lines were added to the plot including that at mean differences and the upper and lower limits of agreement (LOA).

Deming regression analysis and Scatter plots for the corneal epithelial thickness between the software output and the manual measurements are provided for the Combined Group and the 5 sub-groups. Deming regression analysis on corneal epithelial thickness for the Combined Group is also provided, including intercept, confidence intervals (CI) of intercept, slope, and confidence intervals (CI) of slope.

Conclusions From Data

The conclusions drawn from the non-clinical verification tests (software, electrical safety, and EMC) and validated by clinical studies demonstrate that the iVue subject device with modified software is as safe and as effective as the legally marketed iVue predicate device.