

Review of Normative Database
Construction in
Available OCT Models

Robert Fechtner, MD

Disclosure

No financial interest in any of the content of this presentation.

What's in a word?

- Normative database
- Reference database

What is the database for?

- Serves as a reference for new examinations
- Can determine a percentile rank for a calculated (measured) parameter (like a test score on a standardized test)
- It is a tool and results must be interpreted in a clinical context

What the database can answer

- In what percentile does the measurement fall compared with the reference population?

What the database cannot answer?

- Does one have disease or not?
- Normal, borderline, abnormal (in any other than a statistical sense)
- (But if designed correctly one is more likely to have disease at the tail end of the distribution.)

What is a reference database?

- Who is in the database?
- Who made the decision to include or exclude?
- Based on what criteria?

Resources Accessed

FDA Resources

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>



510(k) Premarket Notification

[FDA Home](#) [Medical Devices](#) [Databases](#)



A 510(K) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR [§807.92\(a\)\(3\)](#)) that is not subject to premarket approval.

[Learn more...](#)

Other Databases

- [510\(k\)s](#)
- [Registration & Listing](#)
- [Adverse Events \(MAUDE\)](#)
- [Recalls](#)
- [Premarket Approvals \(PMAs\)](#)
- [Inspections](#)
- [Device Classification](#)
- [Standards](#)
- [Total Product Life Cycle](#)
- [CFR Title 21](#)
- [Radiation-Emitting Products](#)
- [X-Ray Assembler](#)
- [Medsun Reports](#)
- [CLIA](#)

Search Database

[Help](#) [Download Files](#)

510K Number	<input type="text" value="K"/>	Type	<input type="text"/>
Model	<input type="text"/>	Cleared/Approved IVD Products	<input type="checkbox"/>
Applicant Name	<input type="text"/>	Expedited Review	<input type="text"/>
Device Name	<input type="text"/>	Third Party Reviewed	<input type="checkbox"/>
Panel	<input type="text"/>	Product Code	<input type="text"/>
Decision	<input type="text"/>		
Decision Date	<input type="text"/>	to	<input type="text"/>
		Clinical Trials	<input type="checkbox"/>



510(k) Premarket Notification

[FDA Home](#) [Medical Devices](#) [Databases](#)



1 to 10 of 17 Results
ProductCode: obo

[1](#) [2](#) [>](#)

Results per Page

[New Search](#)

[Export to Excel](#) | [Download Files](#) | [More About 510\(k\)](#)

Device Name	Applicant	510(K) Number	Decision Date
Cirrus Photo	Carl Zeiss Meditec Inc	K112184	06/18/2012
Envisu Spectral Domain Ophthalmic Imagin	Bioptigen, Inc.	K120057	05/11/2012
Cirrus Hd-Oct With Retinal Nerve Fiber L	Carl Zeiss Meditec Inc	K111157	01/19/2012
Spectralis Anterior Segment Module (Spec	Heidelberg Engineering Gmbh	K113129	11/08/2011
Rtvue Cam With Corneal Power Upgrade	Optovue, Inc.	K111505	09/08/2011
Spectralis Hra+Oct, Spectralis Fa oct_S	Heidelberg Engineering	K101223	10/01/2010
Ivue, Model 100	Optovue, Inc.	K091404	04/22/2010
Optical Coherence Tomography 3d Oct-2000	Topcon Corp.	K092470	09/02/2009
Cirrus Hd-Oct With Retinal Nerve Fiber L	Carl Zeiss Meditec Inc	K083291	05/05/2009
3d Oct-1000 Mark II Optical Coherence To	Topcon Medical Systems, Inc.	K083316	03/13/2009

Optovue RTVue

- “The Normative Database for the RTVue” - Michael J. Sinai, PhD (K101505) (software version 6.0)
- FDA Website 510(K) Summary K101505
- Dr. Qienyuan Zhou – personal communication

CZM Cirrus HD OCT

- O'Rese J. Knight et al. Effect of Race, Age, and Axial Length on Optic Nerve Head Parameters and Retinal Nerve Fiber Layer Thickness Measured by Cirrus HD-OCT. Arch Ophthalmol. 2012;130(3):312-318
- FDA Website 510(K) Summary K111157
- Dr. Vincent Michael Patella – personal communication

Heidelberg Spectralis

- Spectralis user guide section 11.8.5
“Normative Database” (page 250-251)
- FDA Website 510(K) Summary K101223
- Dr Gerhard Zinser – personal communication

Database Subject Collection

	RTVue	Cirrus	Spectralis
Study Sites	11 worldwide contributed data (15 initially recruited): 6 USA 3 Japan 1 India 1 England	6 USA 1 China	1 Germany
# Subjects	480	284	201
Subject Ethnicity	Caucasian African descent Hispanic Asian Indian other	African descent Chinese European descent Hispanic	Caucasian
Subject Age	18-84	19-84	18-78
Significance limits include	RNFL thickness Ganglion cell complex (GCC) Macular retinal thickness	peripapillary RNFL thickness RNFL thickness for the optic nerve head scan cube optic nerve parameters macular ganglion cell + IPL thickness macular retinal thickness	RNFL thickness

Exclusions

	RTVue	Cirrus	Spectralis
Ocular History	<ul style="list-style-type: none"> active ocular disease congenital abnormalities anatomic narrow angle glaucoma or suspect diabetic retinopathy uncomplicated cataract surgery within 6 month other previous intraocular surgery 	<ul style="list-style-type: none"> vitreo-retinal disease, uncomplicated cataract and/or refractive surgery eye within 12 months any complicated eye surgery amblyopia glaucoma, ocular hypertension, glaucoma suspect angle closure, disc hemorrhage infection or inflammation in the eye 	<ul style="list-style-type: none"> Glaucoma vitreal, retinal or choroidal diseases or disease of the optic nerve any intraocular disease prior intraocular surgery (except cataract surgery)
Medical History	<ul style="list-style-type: none"> leukemia AIDS dementia multiple sclerosis arteriosclerosis 	<ul style="list-style-type: none"> leukemia AIDS dementia multiple sclerosis diabetes mellitus uncontrolled systemic hypertension 	<ul style="list-style-type: none"> diabetes mellitus
Family History	<ul style="list-style-type: none"> glaucoma 1st degree relative 		
Medication	<ul style="list-style-type: none"> hydroxychloroquine or chloroquine 		

Examination Parameters

	RTVue	Cirrus	Spectralis
Refraction	outside +/- 8 D sph, +/- 2 D cyl	outside -12 D to +8 D sph	outside -7 D to +5 D sph
IOP	< 22 mmHg	< 22 mmHg	≤ 21 mmHg
Visual Acuity	BCVA 20/30 or better in each eye	no less than 20/40 Snellen or Snellen equivalent either eye	0.7 or better (~20/30)
Optic nerve and RNFL	The appearance of the optic disc was not used as an exclusion criterion	no disc hemorrhage, RNFL defects	normal appearance of optic disc - 2 examiners
Visual Field	normal Humphrey 24-2 white on white test (<25% FN, FP, FL) normal GHT (normal Octopus visual field also accepted)	normal Humphrey 24-2 Visual Field (15% or less FN, FP, FL) (normal program 30-2 also accepted)	Normal visual field based on FDT, Octopus or Goldman perimetry

Structure

 Normal

 Borderline

 Abnormal

Function

∴ < 5%

⊗ < 2%

⊠ < 1%

■ < 0.5%

△ P < 5% DETERIORATION

▲ P < 5% (2 CONSECUTIVE)

▲ P < 5% (3+ CONSECUTIVE)

X OUT OF RANGE

Structure?

 $\geq 5\%$

 $< 5\%$

 $< 1\%$

The Question of Generalizability

Example

The Cirrus HD-OCT normative database comprised 284 subjects of 527 subjects screened for inclusion.

240/527 (46%) were disqualified for the following reasons:

138/527 (26%) abnormal or unreliable visual field examination findings

40/527 (8%) posterior pole pathology

30/527 (6%) study-related medical issues

Have we sufficiently
re-examined assumptions
underlying current approach?

Who should be included?

Can/should optic nerve abnormality be an exclusion?

Who should be included?

Should medical conditions be an exclusion?

Who should be included?

Is visual field required? What is normal?

The more exclusions, the greater the
chance of a “supernormal” reference
population

Is this desirable?

Why not be inclusive?

Would predictably improve
specificity.

What if all were included?

- Unbiased population-based cohort
- Some with disease would be included
- Reference database would still resemble general population if large enough and disease with low prevalence
- Remains a percentile measure

Reference Database

- Serves as a reference for new examinations
- Can determine a percentile rank for a calculated (measured) parameter (like a test score on a standardized test)
- It is a tool and results must be interpreted in a clinical context

The value of expert consensus

- Expertise resides in FDA and AGS
- Provide guidance for acceptable reference database construction
- Some basic questions must be addressed
- Model protocol for a basic reference database

WORLD GLAUCOMA CONGRESS



Vancouver Convention Centre
Vancouver, Canada
July 17-20, 2013

www.worldglaucoma.org



Nov. 1, 2012 – Abstract Submission Opens

WORLD GLAUCOMA ASSOCIATION
The Global Glaucoma Network