The OCT in Retina and Glaucoma

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Optical Coherence Tomography (OCT)

- Non-contact, non-invasive imaging device
- Produces high-resolution images of the posterior segment
  - Optical biopsy
- Images are objective and quantifiable

Optical Coherence Tomography (OCT)

- Major advancement in the evaluation of ocular conditions especially retinal
- Now readily available in most areas
  - Only available in a few major medical centers prior to 2000
- Considered the “Standard” for imaging technology

History of the OCT


Original Founders:
- David Huang, MD, PhD student at Harvard-MIT
  - Conceived the idea of OCT while working with Dr. James Fujimoto, PhD
- Eric Swanson, MS built the 1st OCT at the Lincoln laboratory of MIT
- Carmen Puliafito, MD
- Formed startup company: Advanced Diagnostics

The Origins of the OCT

- 1996 OCT1 debuted at 100 axial scans per second
- 2002 The Stratus OCT was introduced and quadrupled the speed 400 axial scans per second
- Stratus became the standard for the diagnosis of many retinal diseases and glaucoma
- Utilizes time domain technology

Optical Coherence Tomography (OCT)

- Based on principle similar to ultrasound
- Uses Low coherent light waves rather than sound
- Light allows higher resolution (maximum of approximately 10 microns)
- Image produced based on acoustic reflectivity properties and interference patterns from the various ocular tissues
Advantages of OCT

- Quick – takes less than five minutes to obtain images of both eyes
- Non-invasive and well tolerated by patients
  - No injection
  - No biohazard or blood-related risk
  - No medication reactions
- More readily interpreted and understood by patients

Main Clinical Utilities of OCT

- High resolution evaluation of retinal anatomy
- Diagnosis of macular conditions difficult to establish with biomicroscopy
- Quantitative assessment of retinal anatomic alterations
- Quantitative assessment of vitreoretinal interface
- Objective means for monitoring disease progression and/or therapeutic response

Diagnosis of macular conditions difficult to establish with biomicroscopy
50 y/o Creole Female

Decreased vision OU L > R X 6 months

Full Thickness Macular Hole

Vitreomacular Traction
Impending Macular Hole

AMD with CNV
Macular Edema

Classic Choroidal Neovascularization

Inferior Superior

VA = 20/300

Post-Operative Cystoid Macular Edema

VA = 20/100

Early Late

CME

VA = 20/100

Temporal Nasal

Idiopathic Central Serous Chorioretinopathy

VA = 20/400

Early Late

Idiopathic Central Serous Retinopathy
**Breakthroughs with OCT**

**Provided New Perspectives in the Understanding of Vitreoretinal Macular Disease**
- It has redefined our understanding of the pathogenesis of macular hole formation and
- Expanded the spectrum of vitreomacular traction

**Idiopathic Macular Holes**
- Females 70%
- 6th to 7th decade
- No predisposing factors
- Blurred VA
- Metamorphopsia
- Develops from perifoveal vitreous detachment

**Stages of Macular Holes**
Stages of Macular Holes

0: Stage “0” macular hole
I: Pseudocyst associated with traction
   IA: Yellow spot or ring in macula
   IB: Loss of foveal depression
II: Partial tear in the sensory retina
III: Full thickness macular hole
IV: Macular hole with PVD

Vitreomacular Traction

- Originally described as a “syndrome”
- Incomplete or partial PVD at the ON
- Results in traction at the macula
  - Often in a “dumbbell” shaped configuration
- Produces macular edema – CME
- Necessitates pars plana vitrectomy
- Rare

Smiddy, Green, Michaels AJO, 1989

Vitreomacular Traction in the Era of OCT

- Not rare!
- A group of disorders caused by incomplete PVD
- Leads to persistent traction on the macula
- Produces in most cases CME and decreased visual acuity
- Can be idiopathic
- Can occur with ERM and macular hole

Optical Coherence Tomography (OCT)

- Greatly enhances our ability to identify vitreomacular traction
  - Represents traction at the macula from incomplete PVD
- VMT is more common than previously suspected
- Improved understanding of the pathogenesis of macular holes
- Excellent clinical tool for the evaluation and management of these conditions
Next Generation OCT

Spectral-Domain OCT (Fourier Domain OCT)
- Does not utilize a mirror
- Analyzes data using a spectrometer
  - Allows the ability to determine various depths simultaneously – current OCT does this serially
- Very fast acquisition speed -> 100 X > acquisition speed (1.28 for current vs milliseconds)
- Very high resolution – 3.5 to 6 µ
- 3-D imaging

Spectral Domain OCT

The Competition
- Carl Zeiss: Cirrus
- OptiVue: RTvue
- Heidelberg: Spectralis
- Topcon

The evolution of OCT

Cirrus™ HD-OCT
- A new member of the Zeiss OCT family of products
- Spectral domain OCT technology
- Capable of volumetric (3D) & high definition line scanning of the retina
- Received FDA 510K clearance February 2007
- Available in the fall of 2007
Time Domain and Spectral Domain

Stratus OCT™ high-resolution line scan and the Cirrus HD-OCT scan reveal details of retinal structure.

High Definition and High Resolution

Axial resolution or definition determines which retinal layers can be distinguished. Axial resolution is determined by the light source.

Transverse resolution determines accuracy with which size and separation of features (such as drusen) can be identified. Transverse resolution is determined by optics of the eye, as limited by pupil size, and as corrected by the scanner.

Normal Male

Yellow square on LSLO fundus image represents the 6mm x 6mm margins of the scanned macular cube. Adjustable cross hair on fundus image shows precise location of the horizontal and vertical scans selected.

Normal Male

Precise location of raster lines indicated on LSLO fundus image.

Normal Male

LSLO fundus image with overlay of retinal thickness map. 3D layer segmentation maps provide detailed visualization of histology and pathology.

Cirrus HD-OCT Image of Schisis

Cirrus™ HD-OCT Image of Schisis: 3D segmentation of ILM and RPE layers.
AMD with Drusen

38 Year-Old Male, High Myopia with ICSC

Yellow square on LSLO fundus image represents the 6mm x 6mm margins of the scanned macular cube
Adjustable cross hair on fundus image shows precise location of the horizontal and vertical scans selected.

Vertical B-scan comprised of 128 A-scans
Horizontal B-scan comprised of 512 A-scans

Precise location of raster lines indicated on LSLO fundus image

Scan alignment to previous visit

LSLO fundus image with overlay of retinal thickness map
3D layer segmentation maps provide detailed visualization of histology and pathology

3D retinal thickness map 3D segmentation of RPE layer 3D segmentation of ILM and RPE layers

3D segmentation of ILM and RPE layers
What is Advanced Visualization?

- Visualization of cube data in 3 dimensions beyond dynamic 3D cube analysis
- Averaging/Mean imaging of user-defined C-Scan groupings referred to as “Slabs”
- With “Slab” analysis, user can image 2D en face representations of common retinal layers/disorders:
  - Choroidal Vasculature
  - RPE/NSR
  - Vitreoretinal Interface
  - Epiretinal Membrane
  - Choroidal Neovascularization
  - Pigment Epithelial Detachment
  - Intraretinal Cystic formations

Advanced Visualization

- The Tissue Layer image allows you to isolate and visualize a layer of the retina.
- The thickness and placement of the layer are adjustable.
- This provides a virtual dissection of the retina by extracting the layer of interest.

En face view of RPE layer

Advanced Visualization

- The RTVue 100
  High Speed, High Resolution OCT
Fourier Domain OCT – RTVue 100

- Optical Coherence Tomography provides cross sectional imaging of the retina
- Spectrometry and Fourier Domain methods allow high speed data capture (26,000 A scans per second)
- Broad-band light source provides high depth resolution (5 microns)

High Speed allows 3-D scanning

B-scans provide high resolution detail

Macula thickness map reveals edema

Cystoid Macula Edema

Classic CNV
Spectralis™
HRA+OCT

The Fusion of Imaging Technologies

SPECTRALIS Technology
- Combined *confocal* scanning laser ophthalmoscope and spectral domain OCT
- Built on a *fundus imaging* platform
- Combines high resolution cSLO C-scan with high resolution SD-OCT B-scan
- Scans with TruTrack™ Eye Tracking
- Incorporates Heidelberg Noise Reduction™

Eye Tracking using TruTrack®

Scan does not follow eye  
Scan tracks with eye

Eye Tracking Stops 3D Motion Artifact

Without Eye Tracker  
With Eye Tracker

Artificial ripples due to eye movements  
True anatomic structure

Topcon 3D-OCT

No glaucoma data base

OCT in Glaucoma
Traditional Methods of Assessing Glaucoma
- IOP monitoring
- Major risk factor
- Subjective evaluation of the optic nerve
- Visual field testing

There is a need for objective testing that can reliably detect those patients who may have glaucoma and/or are at risk of developing glaucoma.

Structural Assessment Instruments
“According to the AIGS, there is limited but consistent evidence that automated imaging systems can detect early to moderate glaucoma equally as well as standardized, expert qualitative assessment of stereoscopic optic disc and RNFL photographs in clinical research settings.”

OCT: Glaucoma and NFL Analysis
- Multiple studies show that OCT has the ability to detect early glaucoma change by measuring NFL thickness
- Often before visual field loss

What is the science that supports this?

Value of OCT in Glaucoma
- RNFL analysis
- Optic nerve head topography
- Bilateral comparisons
- Serial comparison
- Normative database

Retinal Nerve Fiber (RNFL) Analysis
- Circular scans around the ONH at radius of 1.73 mm
- Scans begin temporal
- 3 scans are acquired and data is averaged
Standard or Fast

- Standard
  - More scans more data points
  - 512 scans 1536 data points
- Fast
  - Fewer scans - as good sensitivity
  - 256 scans 768 data points
  - Normative database

RNFL Measurement

- Measures differences in delay of the backscattering of light from the RNFL
- RNFL is differentiated by an algorithm that detects anterior edge of the RPE and the photoreceptor layer position

RNFL Thickness Analysis With Normative Data

- Analysis results displayed in tabular display and graphs
- RNFL thickness graph in TSNIT orientation with normative data display
- Asymmetry demonstrated in OU TSNIT graph
- OD RNFL thickness within normal limits (green)
- Scan image
- Scan signal strength and quality
- OS areas of RNFL outside normal limits (red)

Normative Database

- Provides age-matched reference values for retinal nerve fiber layer thickness measurements
- FDA approved July 2003
- Fast RNFL thickness scans 256 points
- > 350 subjects; age 20-80, mean age 47
- 6 sites in US
- Broad representation of ethnic group
- No correlation for other demographic factors such as ethnicity or gender, right/left eye

Stratus OCT Stop Light Display of RNFL Normative Range

- 95% of normal population falls in or below green band; 90% falls within green band
- 4% of normal population falls within or below yellow band; 4% falls within the yellow band
- 1% falls within red band; considered outside normal limits

Normal Distribution Percentiles

- 100%
- 95%
- 5%
- 1%
- 0%
RNFL in Glaucoma

“False” Positive and Negatives
- High Myopia
- Optic nerve tilt
- Peripapillary atrophy
- Disc drusen
- Sectoral pigmentary changes
- Retinal edema
- Retinal cystic changes
- Retinal traction
- ERM
- Myelinated nerve fibers
- Optic nerve pit

Assessing Data Points

Any change repeatable > 12µm is statistically significant

Inferior and Superior RNFL Averages
- Superior RNFL Ave = 142.7µm
  - Early Glaucoma = 104.8µm
- Inferior RNFL Ave = 138.6µm
  - Early Glaucoma = 103.9µm

Normal Patient

Glaucoma Patient

How good is OCT as Diagnosing Glaucoma…

…or Detecting Progression

RNFL Sensitivity and Specificity of the OCT for Diagnosing Glaucoma

Budenz et al Ophthalmology. January 2005;112:3-9

- 109 normal and 63 glaucoma subjects
  - 18 mild, 21 moderate, 24 severe (VF)
- Avg RNFL < 5% 84% sensitivity; 98% specificity
- ≥1 or more quad <5% 89%, 95%
- ≥1 or more clock hours <5% 89, 92%
- Inferior and superior sectors and quadrants better than others

Sensitivity and Specificity of Stratus OCT

<table>
<thead>
<tr>
<th>OCT Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
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</thead>
<tbody>
<tr>
<td>Ave RNFL Thickness &lt; 5%</td>
<td>84% (75-93%)</td>
<td>98% (96-100%)</td>
</tr>
<tr>
<td>Ave RNFL Thickness &lt; 1%</td>
<td>68% (57-80%)</td>
<td>100%</td>
</tr>
<tr>
<td>≥1 Quad with Ave RNFL Thickness &lt; 5%</td>
<td>89% (81-97%)</td>
<td>95% (90-99%)</td>
</tr>
<tr>
<td>≥1 Clock Hr with Ave RNFL Thickness &lt; 5%</td>
<td>83% (73-92%)</td>
<td>100%</td>
</tr>
<tr>
<td>≥1 Clock Hr with Ave RNFL Thickness &lt; 1%</td>
<td>89% (81-97%)</td>
<td>92% (87-97%)</td>
</tr>
</tbody>
</table>

Correlation of RNFL Thickness to Having Glaucoma

- Inferior Quadrant 0.971
- Mean 0.966
- Inferior Temporal 0.959
- Superior Quad 0.952

Rogelia 62 y/o Hispanic Female

- CC -> pain/burning in the both eyes c/w dry eye
- VA: 20/20 OU
- Ant Segment unremarkable
- TA: 12 OU
- Fundus

Rogelia - Summary

- 63 y/o Hispanic Female presents with dry eye complaints
- Suspicious Cups RE inferior thinning and a superior nasal field defect RE (Normal LE), consistent with OCT RNFL findings, IOP 12
- Diagnosis -> NTG RE, No GL LE
- Management…initial observation until documented progression…then Tx
Ability of OCT to Detect Localized RNFL Defects


- 55 Patients – 43 NTG, 12 POAG with visible wedge-shaped RNFL Defects and corresponding VF defects
- The OCT showed good diagnostic agreement with red-free RNFL photos
- Sensitivity of 85.9%; Specificity of 97.4% with normative data base

Reproducibility of OCT RNFL Measurements


- Same day reproducibility of RNFL measurements of glaucoma and nonglaucomatous eyes using OCT
- Excellent reproducibility in both groups
  - Normal range was 3.5µ-4.7µ
  - Glaucoma range was 5.2µ-6.6µ
- Nasal quadrant has most variability
  - 10.2µ-13.0µ Normals vs. 10.2µ-13.8µ glaucoma

Documenting Progression with OCT Serial Analysis

Excellent Reproducibility On Both Visits
Documenting Progression with OCT

Serial Analysis


- 75 pts with glaucoma, 66 normals
- 70% had early GL visual field loss
- No Statistical difference b/w the 3 machines
  - Stratus OCT 0.92
  - GDX 0.91
  - HRT II 0.86

Sensitivity/Specificity Between Instruments

Agreement Between Instruments


- OCT and GDX VCC: 89% agreement
- GDX VCC HRT II: 81% agreement
- HRT II and OCT: 81% agreement

†HRT measures optic disc topography and provides indirect measurement of RNFL as a secondary

Cirrus™ HD-OCT

Software Version 3.0

- RNFL Thickness Analysis
- RNFL Normative Data
- 3D Volume Rendering
- Custom 5-line Raster Scan
- High Definition Cross Scan
- Segmentation Editing Tool
- Precise registration

Cirrus Software Version 3.0
Glaucoma – RNFL Thickness Analysis

- Center of disc is automatically identified for precise registration and repeatability
- RNFL thickness display is of a 1.73mm radius circle around the disc
- TSNIT graph is compared to normative database of about 300 patients

Glaucoma – RNFL Thickness Analysis

The LSO fundus image is shown with an OCT fundus overlay. The red circle indicates the location of the RNFL TSNIT circle

The OCT image is a cross section of the TSNIT circle

RNFL thickness is displayed in graphic format and compared to normative data

Glaucoma – RNFL Thickness Analysis

The RNFL thickness map shows the patterns and thickness of the nerve fiber layer

The RNFL deviation map is overlaid on the OCT fundus image to illustrate precisely where RNFL thickness deviates from a normal range

Glaucoma – RNFL Thickness Analysis

An OU analysis example (1)

An OU analysis example (2)

Glaucoma Package
Heidelberg Spectralis
Basic Glaucoma - Circle Scan Analysis
Spectralis: Samples 1536 A-Scans vs. 256 with Cirrus and Stratus

Phase 1 Glaucoma Package

Posterior 30° Pole Analysis
• Full thickness
• Grids correspond to VF
• Hemisphere analysis

Posterior Pole Assessment

RTVue Glaucoma Package

Glucoma Analysis with the RTVue: Nerve Head Map
Provides
• Cup Area
• Rim Area
• RNFL Map

16 sector analysis compares sector values to normative database and color codes result based on probability values (p-values)

Color shaded regions represent normative database ranges based on p-values
Glaucoma Analysis with the RTVue:
Nerve Head Map Parameters

RNFL Parameters

Optic Disc Parameters

All parameters color-coded based on comparison to normative database

The ganglion cell complex (ILM – IPL)

Inner retinal layers provide complete Ganglion cell assessment:
• Nerve fiber layer (g-cell axons)
• Ganglion cell layer (g-cell body)
• Inner plexiform layer (g-cell dendrites)

Early Glaucoma

Borderline Sector results in Superior-temporal region

Abnormal parameters

TSNIT dips below normal

TSNIT shows significant Asymmetry

GCC Analysis may detect damage before RNFL

GCC and RNFL analysis will be correlated, however GCC analysis may be more sensitive for detecting early damage

OCT Glaucoma Summary

- OCT is able to accurately detected early glaucoma with good reliability
- Also very good with already established glaucoma
- Determining same day reliability is critical
  - Corroborate your findings
  - To be to accurately utilize serial analysis in future scans
- OCT is as good as other ON imaging devices

OCT Retina: Summary

- “New” technology allows for cross-sectional imaging of retina structures
- Allows detailed imaging of retinal pathology
- Redefined our understanding of a number of disease processes
- The next generation of imaging - Spectral-Domain OCT is already here