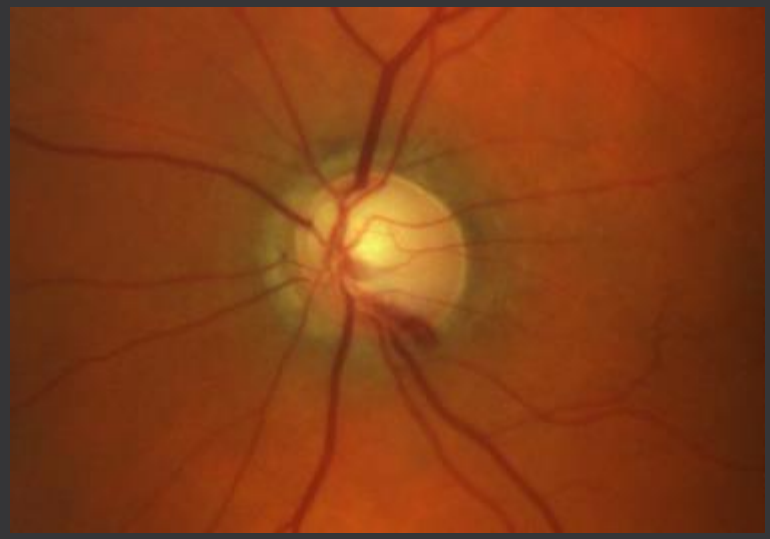
OCT in the management of glaucoma

COPE Course ID: 85636-GL



Andrew J Di Mattina, OD, FAAO

Chief, Greenville HCC Eye Clinic

Greenville, NC

Conflicts

- **I have no conflicts of interest in this lecture.**

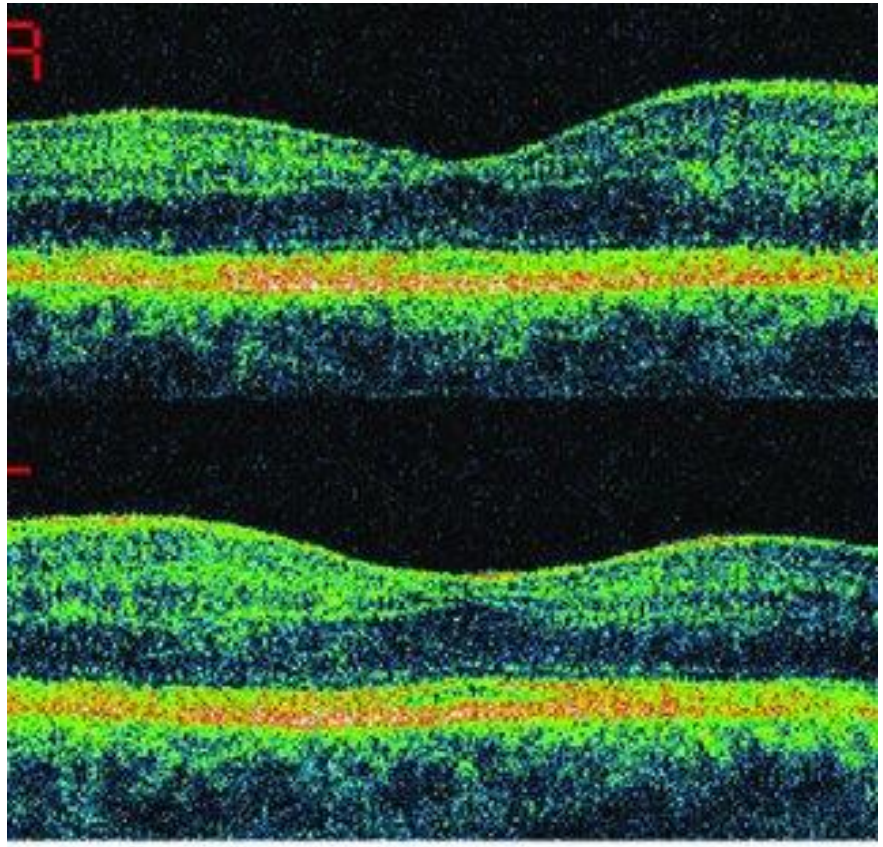
Questions to ask when using OCT in glaucoma management

- **What information am I looking for and what scan(s) do I need to use to get that information?**
- **Is the information I received from my OCT reliable and what artifacts should I be looking for?**
- **Does the OCT data correlate with my clinical interpretation of the optic nerve and the patient's visual field?**
- **If your patient has confirmed glaucoma, are they progressing and what is the rate of progression?**

Will they lose vision/become visually impaired in their lifetime?*

OCT Technology

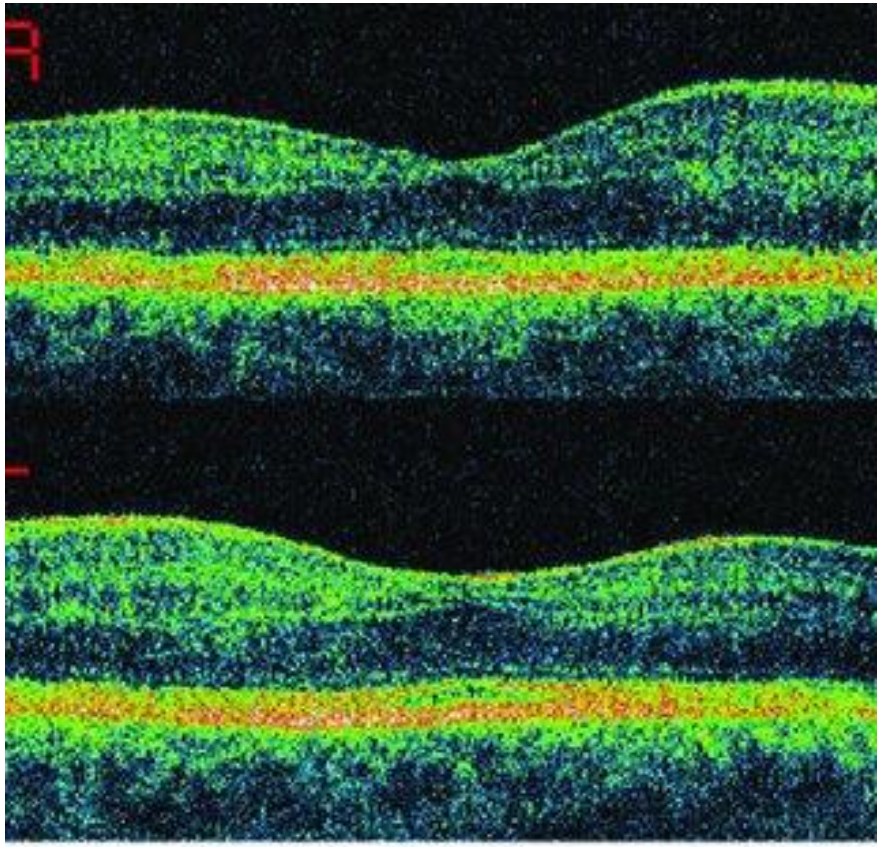
- **Non-contact imaging technique that can assess retinal layers by looking at interference patterns from reflected light**
- **Became commercially available in 1996.**
- **In glaucoma, it provides evaluation of the RNFL, optic nerve head and macula.**



Optical coherence tomography and glaucoma. Annu Rev Vis Sci. 2021 September 15;7:693-726

OCT Technology

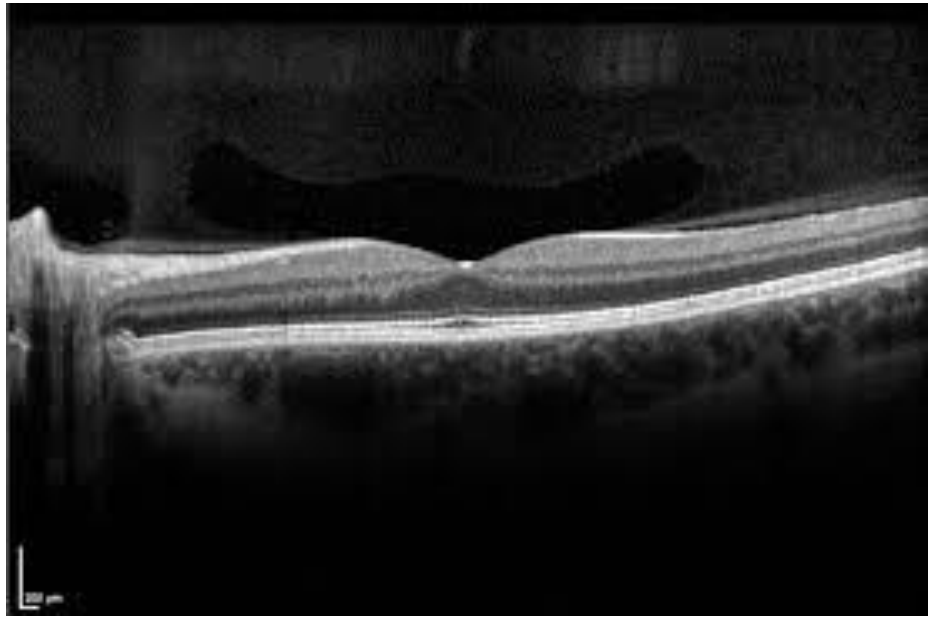
- **Started as time-domain OCT**
  - **Used Near infrared light (NIR)**
  - **Dependent on a mirror to change the optical path of a reference beam**
  - **Top scanning speed was 400 axial scans/second**



Optical coherence tomography and glaucoma. Annu Rev Vis Sci. 2021 September 15;7:693-726

OCT Technology

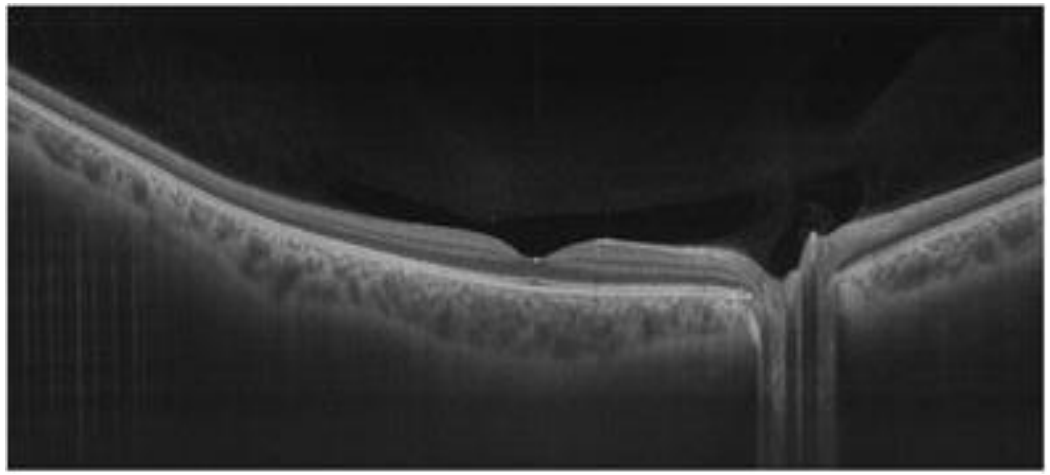
- **Spectral domain OCT was introduced in 2001**
  - **Evaluated the frequency spectrum of the interference between a stationary reference mirror and the reflected light**
  - **Scans up to 100,000 a-scans/second**
  - **Because scanning is faster, fewer motion errors**
  - **Increased signal to noise ratio compared to Time domain, meaning enhanced image quality**



Optical coherence tomography and glaucoma. Annu Rev Vis Sci. 2021 September 15;7:693-726

OCT Technology

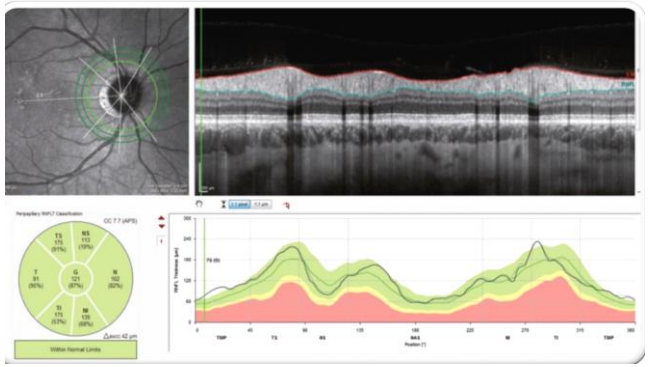
- **Swept Source OCT**
  - **Uses a laser that quickly sweeps through the frequencies at a broad spectrum**
  - **The interference pattern is captured by a photodetector (SD-OCT uses a spectrometer)**
  - **Uses a center wavelength of 1,050 nm which allows for better visualization of the choroid**
  - **Produces 200,000 A scans/second**

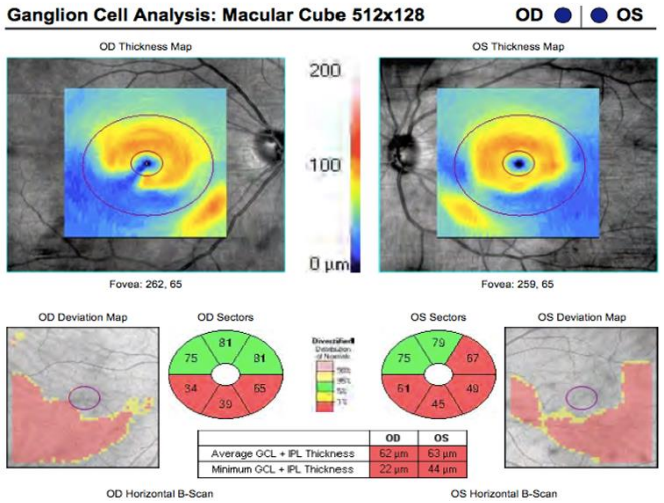


Optical coherence tomography and glaucoma. Annu Rev Vis Sci. 2021 September 15;7:693-726

Question One: What information am I looking for and what scan(s) do I need to use to get that information?

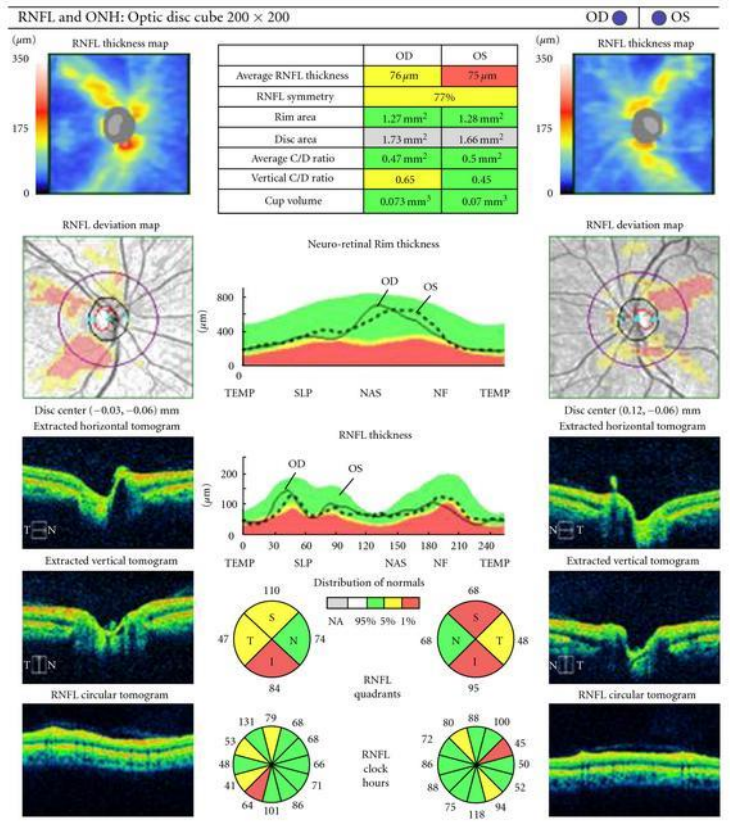
1. RNFL loss
   - RNFL circle scans
   - RNFL cube scans
2. Optic nerve parameters
   - MRW
3. Macular ganglion cell loss
   - Ganglion cell layer
   - GCA
   - GCC
   - Asymmetry analysis
4. Loss of retinal vasculature
   - OCT angiography





RNFL loss

- **Hallmark of glaucoma, as RNFL are the axons from the Ganglion cells.**
- **Often, changes in the RNFL occur prior to visual field loss.**
- **RNFL loss is also present in many other ocular pathologies, so do not look at this scan in isolation.**
- **The patient must have a thorough examination first to look for any other influences on their RNFL loss.**

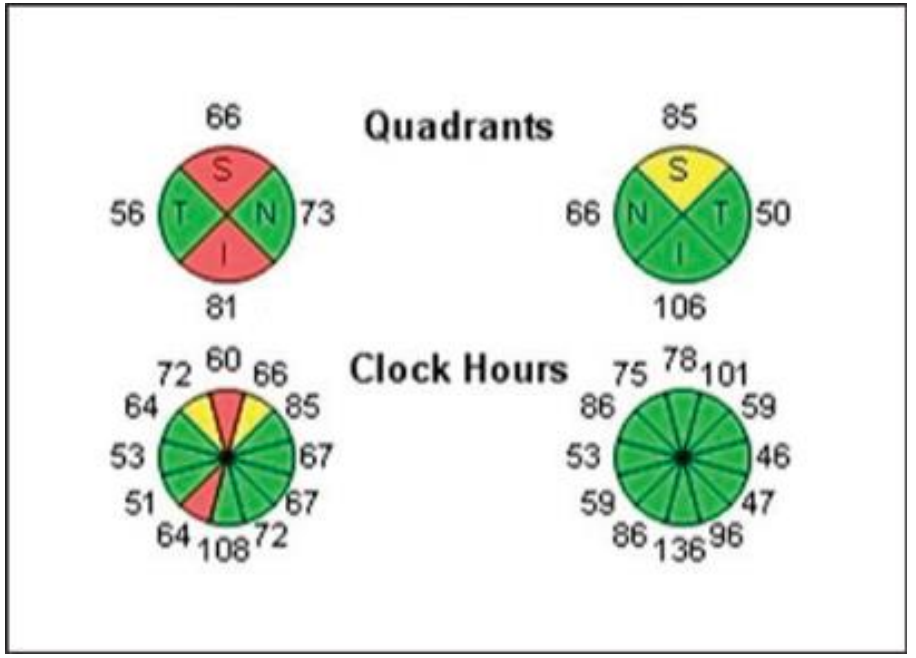


Optic Neuritis

Fiona Costello, "Evaluating the Use of Optical Coherence Tomography in Optic Neuritis", *Multiple Sclerosis International*, vol. 2011

OCT RNFL

- **Remember that reference databases do not diagnose disease.**
- **All the initial scan does is compare the RNFL against a normative database**
- **There are diseased eyes in the "normal' category and normal in the "borderline" or "outside normal limits" categories.**
- **Do NOT treat based solely on this data.**
- **Do NOT release from care based solely on one scan on this data**



- **Green = 95-5% of normative database**
- **Orange= <5% of normative database**
- **Red = <1% of normative database**

Patient Information

Circle Scan

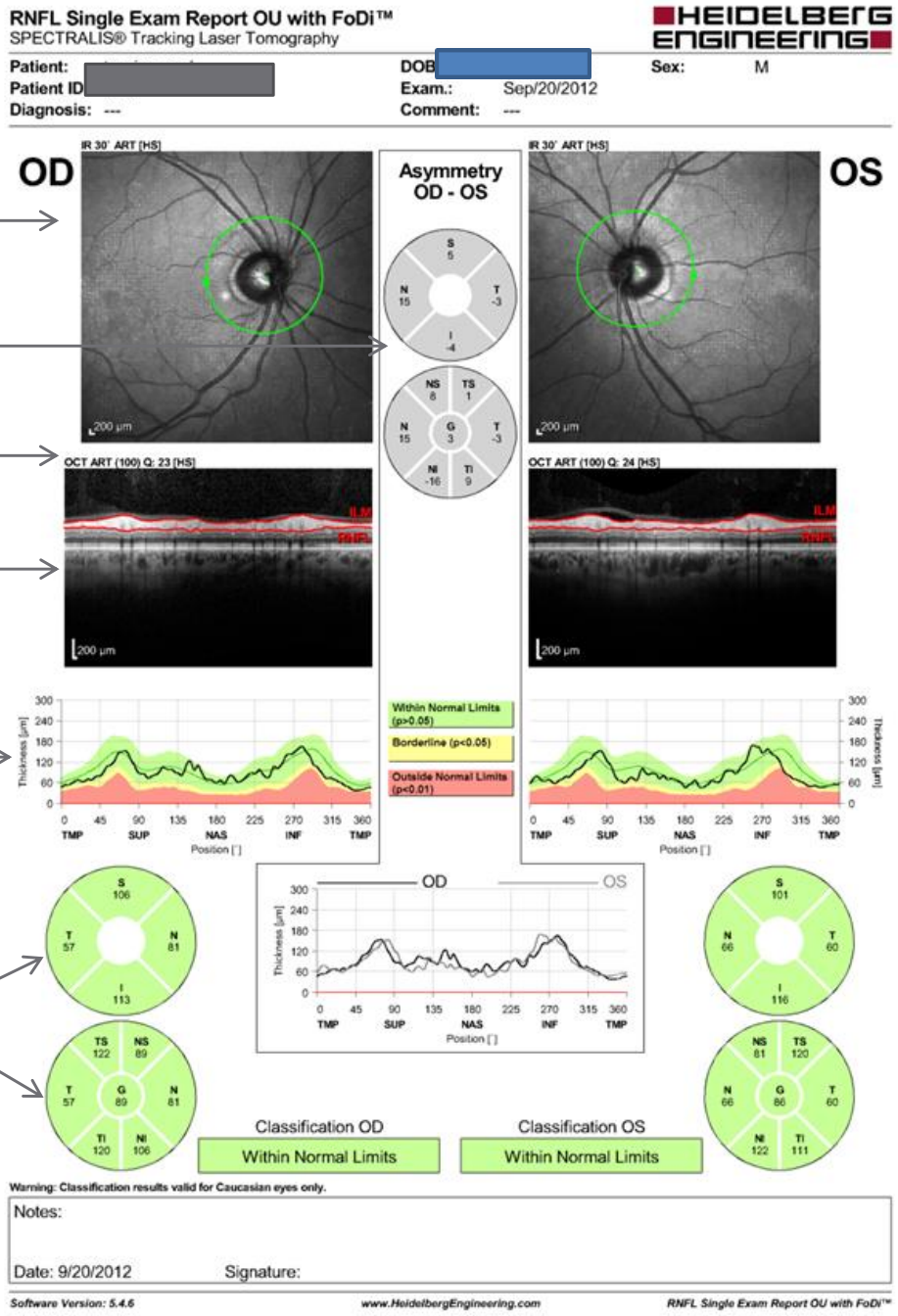
Asymmetry Analysis

Image Quality

OCT scan with automatic Segmentation of RNFL

TSNIT RNFL thickness Compared to normals

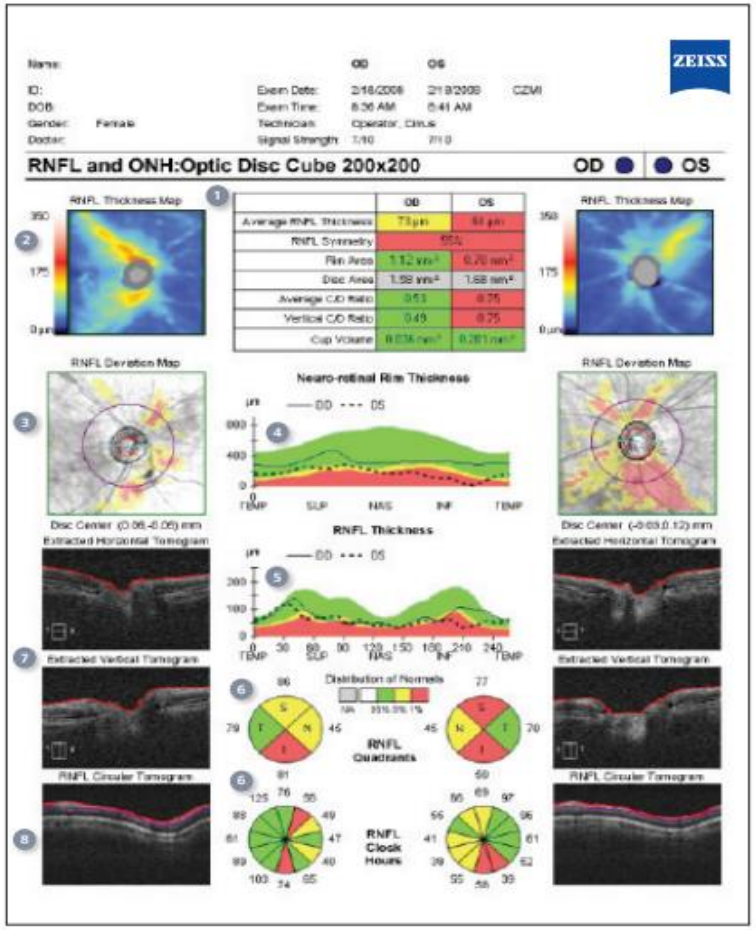
RNFL thickness in quadrants And segments compared to Normative database



Cirrus HD-OCT RNFL and ONH Analysis Report

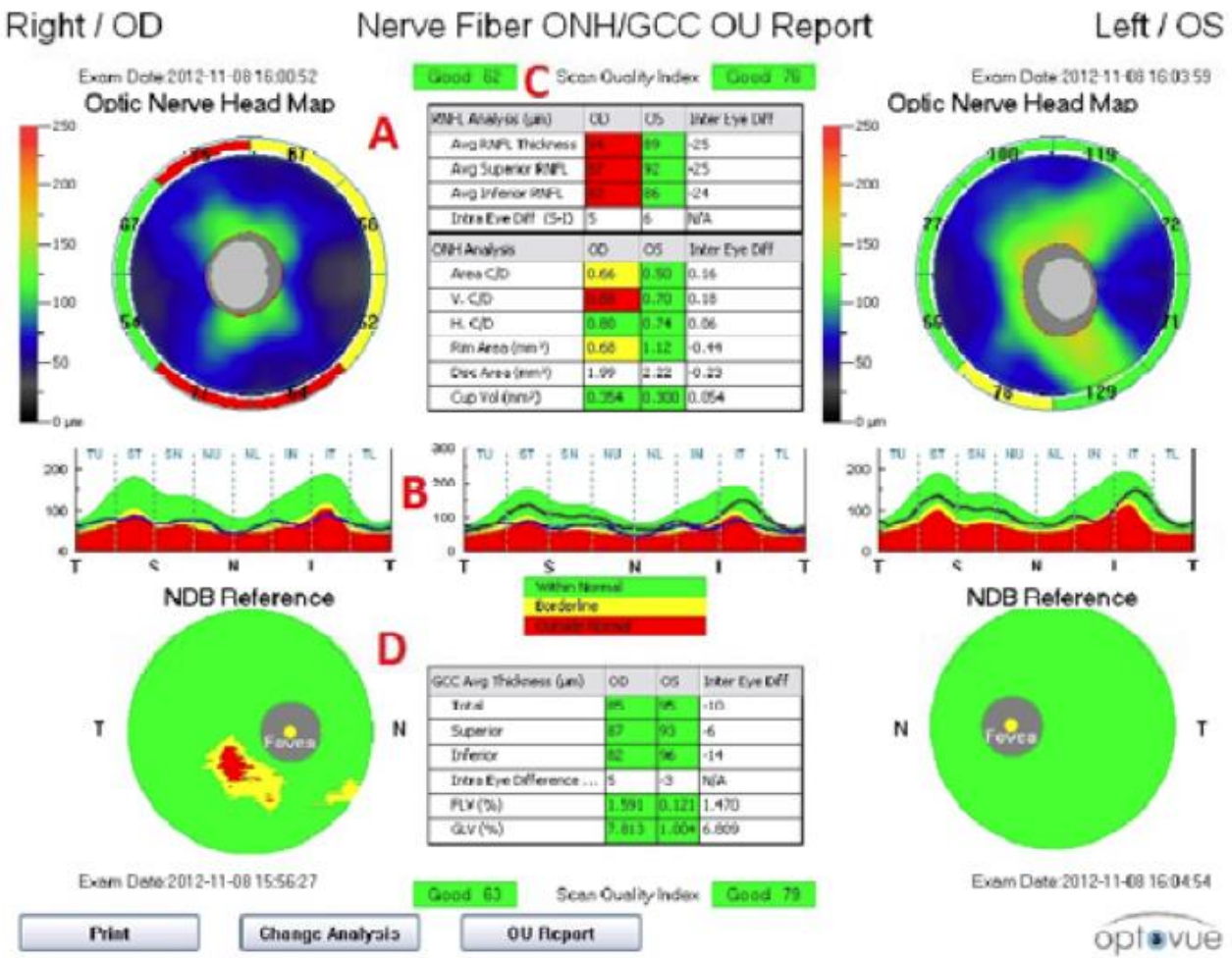
Based on the 6 mm x 6 mm data cube captured by the Optic Disc Cube 200x200 scan, this report shows assessment of RNFL and ONH for both eyes.

1. **Key parameters,** compared to normative data, are displayed in table format.
2. **Nerve Fiber Layer (RNFL)** thickness map is a topographical display of RNFL. An hourglass shape of yellow and red colors is typical of normal eyes.
3. **The RNFL Deviation Map** shows deviation from normal. OCT *en face* fundus image shows boundaries of the cup and disc and the RNFL calculation circle.
4. **Neuro-retinal Rim Thickness** profile is matched to normative data.
5. **RNFL TSNIT graph** displays patient's RNFL measurement along the calculation circle, compared to normative data.
6. **RNFL Quadrant and Clock Hour** average thickness is matched to normative data.
7. **Horizontal and vertical B-scans** are extracted from the data cube through the center of the disc. RPE layer and disc boundaries are shown in black. ILM and cup boundaries are shown in red.



8. **RNFL calculation circle** is automatically centered on the optic disc and extracted from the data cube. Boundaries of the RNFL layer segmentation is illustrated.

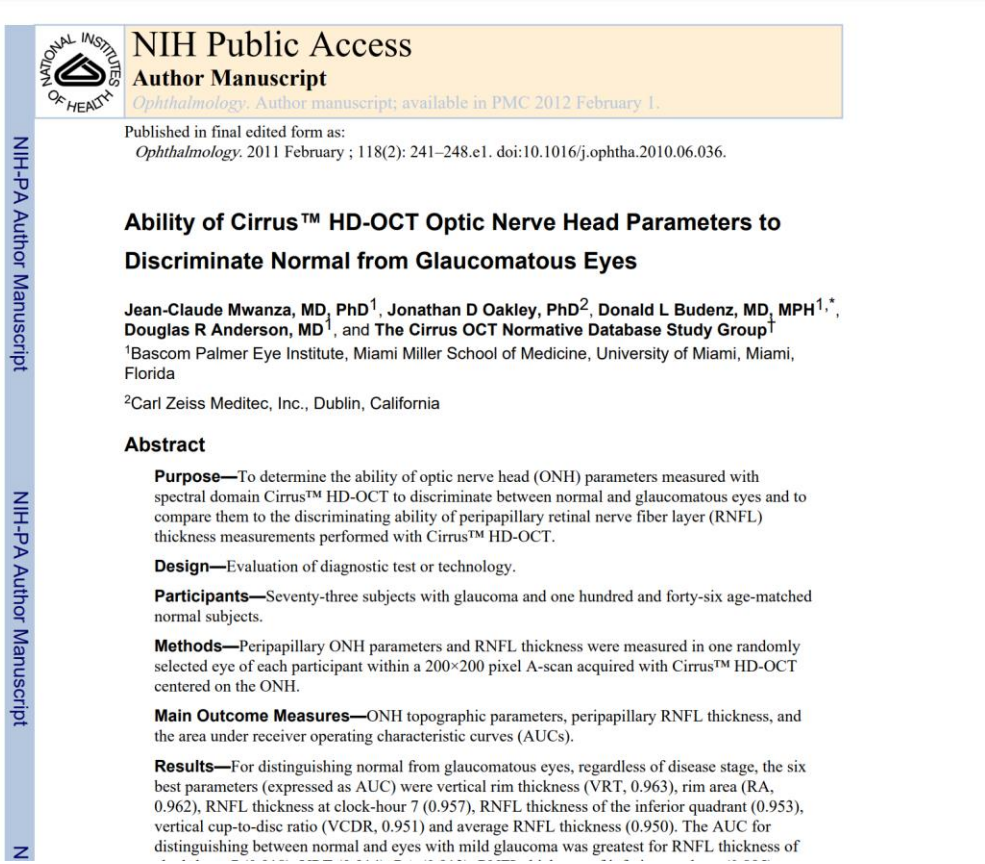
https://www.zeiss.co.uk/content/dam/Meditec/gb/Chris/OCT%20Business%20Builder/PDF%27s/1.pdf



https://www.intechopen.com/chapters/46829

ONH assessment - Zeiss

- **The algorithm identifies the termination of Bruch's membrane as the disc edge.**
- **The rim width around the entire circumference of the optic disc is then determined by measuring the thickness of the neuro-retinal tissue in the optic nerve as it turns to exit through the opening in Bruch's membrane**
- **In the Cirrus OCT normative database study, the Cirrus ONH assessment was found to be able to discriminate normal from glaucomatous eyes, even for mild glaucoma.**



NIH Public Access
Author Manuscript
Ophthalmology. Author manuscript; available in PMC 2012 February 1.

Published in final edited form as:
Ophthalmology. 2011 February ; 118(2): 241–248.e1. doi:10.1016/j.ophtha.2010.06.036.

Ability of Cirrus™ HD-OCT Optic Nerve Head Parameters to Discriminate Normal from Glaucomatous Eyes

Jean-Claude Mwanza, MD, PhD[1], **Jonathan D Oakley, PhD**[2], **Donald L Budenz, MD, MPH**[1,*], **Douglas R Anderson, MD**[1], and **The Cirrus OCT Normative Database Study Group**[†]

[1]Bascom Palmer Eye Institute, Miami Miller School of Medicine, University of Miami, Miami, Florida

[2]Carl Zeiss Meditec, Inc., Dublin, California

Abstract

Purpose—To determine the ability of optic nerve head (ONH) parameters measured with spectral domain Cirrus™ HD-OCT to discriminate between normal and glaucomatous eyes and to compare them to the discriminating ability of peripapillary retinal nerve fiber layer (RNFL) thickness measurements performed with Cirrus™ HD-OCT.

Design—Evaluation of diagnostic test or technology.

Participants—Seventy-three subjects with glaucoma and one hundred and forty-six age-matched normal subjects.

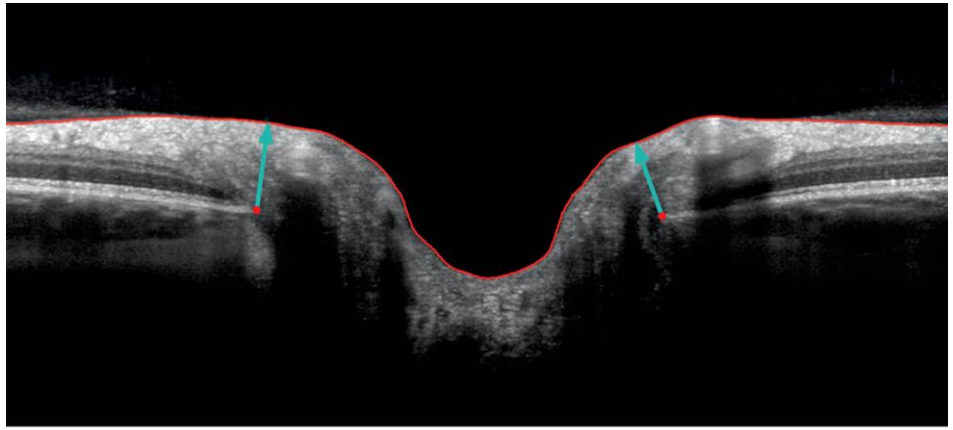
Methods—Peripapillary ONH parameters and RNFL thickness were measured in one randomly selected eye of each participant within a 200×200 pixel A-scan acquired with Cirrus™ HD-OCT centered on the ONH.

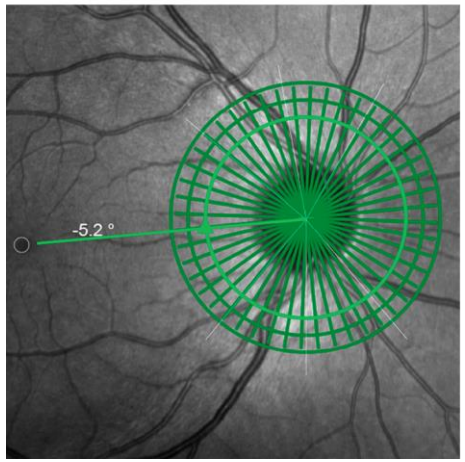
Main Outcome Measures—ONH topographic parameters, peripapillary RNFL thickness, and the area under receiver operating characteristic curves (AUCs).

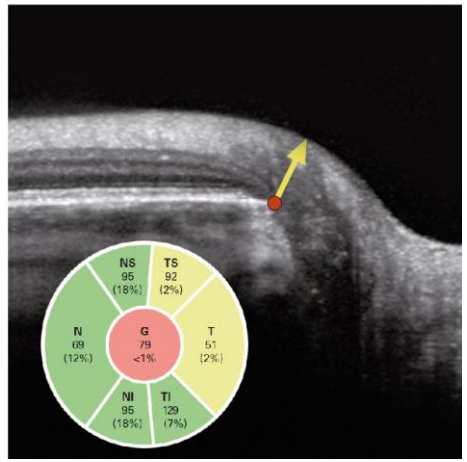
Results—For distinguishing normal from glaucomatous eyes, regardless of disease stage, the six best parameters (expressed as AUC) were vertical rim thickness (VRT, 0.963), rim area (RA, 0.962), RNFL thickness at clock-hour 7 (0.957), RNFL thickness of the inferior quadrant (0.953), vertical cup-to-disc ratio (VCDR, 0.951) and average RNFL thickness (0.950). The AUC for distinguishing between normal and eyes with mild glaucoma was greatest for RNFL thickness of

ONH assessment – Spectralis

- **The Spectralis OCT Glaucoma Module Premium (GMP) Edition uses a different method of ONH analysis using BMO**
- **The neuroretinal rim assessment is performed from the BMO to the nearest point on the internal limiting membrane (ILM), and this shortest distance measurement is referred to as BMO – minimum rim width (BMO-MRW).**
- **This parameter considers the orientation of the rim tissue relative to the point of measurement, the highly variable anatomy of the ONH both within and between individuals, and quantifies the rim width perpendicular to the trajectory of axons.**







Rebolla, G. et al. The new Bruch's membrane opening – minimum rim width classification improves optical coherence tomography specifically in tilted discs. *Clinical Ophthalmology* 2016:10 2417–2425

https://www.businesswire.com/news/home/20160921006167/en/Heidelberg-Engineering-Receives-FDA-Clearance-to-Market-SPECTRALIS%C2%AE-OCT-Glaucoma-Module-Premium-Edition

Bruch's membrane opening and tilted/myopic nerves

- **When imaging healthy patients with moderate myopia, the false positive rate was significantly lower using the BMO-MRW map compared to both Spectralis OCT RNFL and Cirrus macular OCT scans.**
- **Better specificity than RNFL and macular GCA scans for myopic patients.**
- **If you own the Spectralis, it is important to look at the ONH parameter in your myopic glaucoma suspects.**

The new Bruch's membrane opening – minimum rim width classification improves optical coherence tomography specificity in tilted discs

This article was published in the following Dove Press journal:
Clinical Ophthalmology
5 December 2016
Number of times this article has been viewed

Gema Rebolleda
Alfonso Casado
Noelia Oblanca
Francisco J Muñoz-Negrete

Department of Ophthalmology, Hospital Universitario Ramón y Cajal, Madrid, Spain

Background and objective: To investigate and compare the false-positive (FP) diagnostic classification of the Bruch's membrane opening – minimum rim width (BMO-MRW) and retinal nerve fiber layer (RNFL) thickness in healthy eyes with tilted optic disc.

Materials and methods: Fifty healthy eyes of 30 participants with tilted optic disc underwent BMO-MRW and RNFL scanning using Spectralis and macular Cirrus optical coherence tomography (OCT) scans.

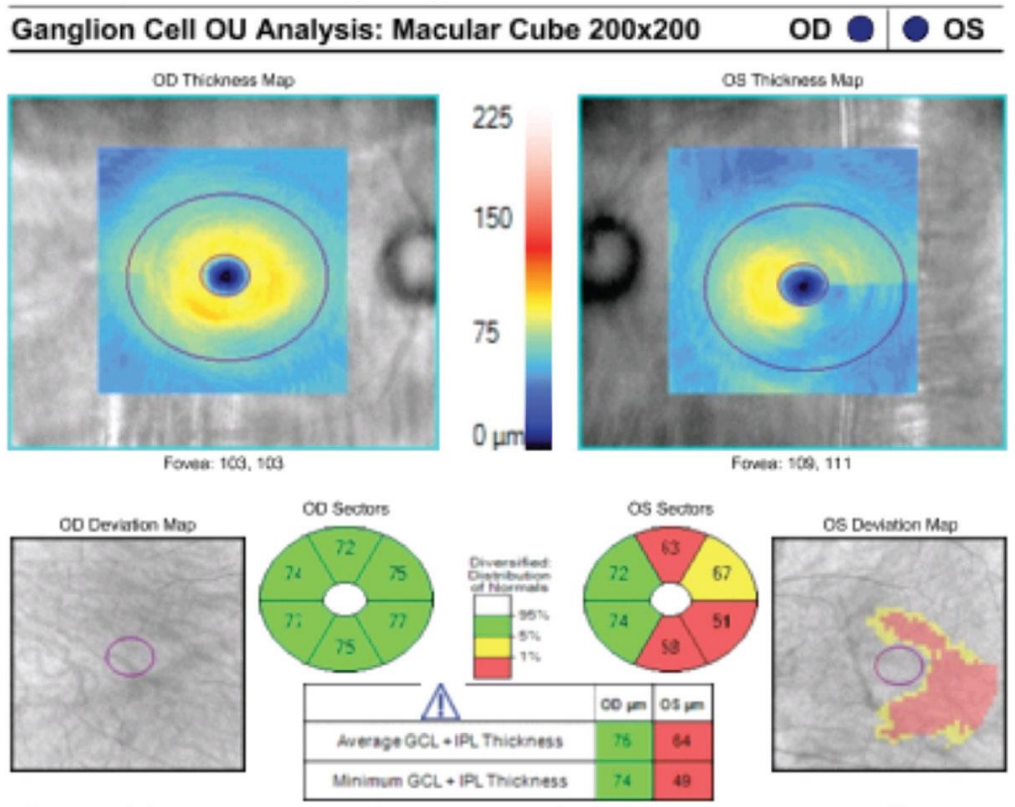
Results: The overall FP rate was significantly lower using BMO-MRW map compared with both RNFL map by Spectralis (8% vs 62%, respectively, $P<0.001$) and ganglion cell analysis (GCA) map by Cirrus (8% vs 50%, respectively, $P<0.001$). Specificity was significantly higher using BMO-MRW than RNFL in eyes with low (89.7% vs 41.4%, $P<0.001$) and moderate myopia (95.2% vs 33.3%, $P<0.001$).

Conclusion: OCT-derived BMO-MRW analysis provides significantly greater specificity than RNFL in tilted disc irrespectively of the refractive error, and it is more specific than GCA analysis in tilted disc with moderate myopia.

Keywords: tilted disc, optical coherence tomography, false-positive, Bruch membrane

Ganglion cell loss

- **Ganglion cell loss is characteristic of glaucoma, so monitoring retinal ganglion cell loss alongside RNFL loss is important in disease detection/progression.**
- **Studies have shown a similar glaucoma diagnostic ability of GCIPL and GCC to RNFL and ONH scans.**



https://www.reviewofoptometry.com/article/the-gangs-not-all-here

- Jeoung JW, Choi YJ, Park KH, Kim DM. Macular ganglion cell imaging study: glaucoma diagnostic accuracy of spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2013;54:4422–4429
- Kotowski et al. Glaucoma Discrimination of segmented Cirrus Spectral Domain Optical Coherence Tomography Macular Scans. Br J Ophthalmol. 2012 November ; 96(11): 1420–1425

Ganglion cell loss in early glaucoma

- **Mwanza et al found improved diagnostic ability for early glaucoma by assessing the all information from RNFL, GCA and ONH parameters vs. using the GCA or RNFL parameters in isolation.**

Diagnostic Performance of Optical Coherence Tomography Ganglion Cell–Inner Plexiform Layer Thickness Measurements in Early Glaucoma

Jean-Claude Mwanza, MD, PhD,[1] Donald L. Budenz, MD, MPH,[1] David G. Godfrey, MD,[2] Arvind Neelakantan, MD,[2] Fouad E. Sayyad, MD,[3] Robert T. Chang, MD,[4] Richard K. Lee, MD, PhD[3]

Purpose: To evaluate the glaucoma diagnostic performance of ganglion cell inner–plexiform layer (GCIPL) parameters used individually and in combination with retinal nerve fiber layer (RNFL) or optic nerve head (ONH) parameters measured with Cirrus HD-OCT (Carl Zeiss Meditec, Inc, Dublin, CA).

Design: Prospective cross-sectional study.

Participants: Fifty patients with early perimetric glaucoma and 49 age-matched healthy subjects.

Methods: Three peripapillary RNFL and 3 macular GCIPL scans were obtained in 1 eye of each participant. A patient was considered glaucomatous if at least 2 of the 3 RNFL or GCIPL scans had the average or at least 1 sector measurement flagged at 1% to 5% or less than 1%. The diagnostic performance was determined for each GCIPL, RNFL, and ONH parameter as well as for binary or-logic and and-logic combinations of GCIPL with RNFL or ONH parameters.

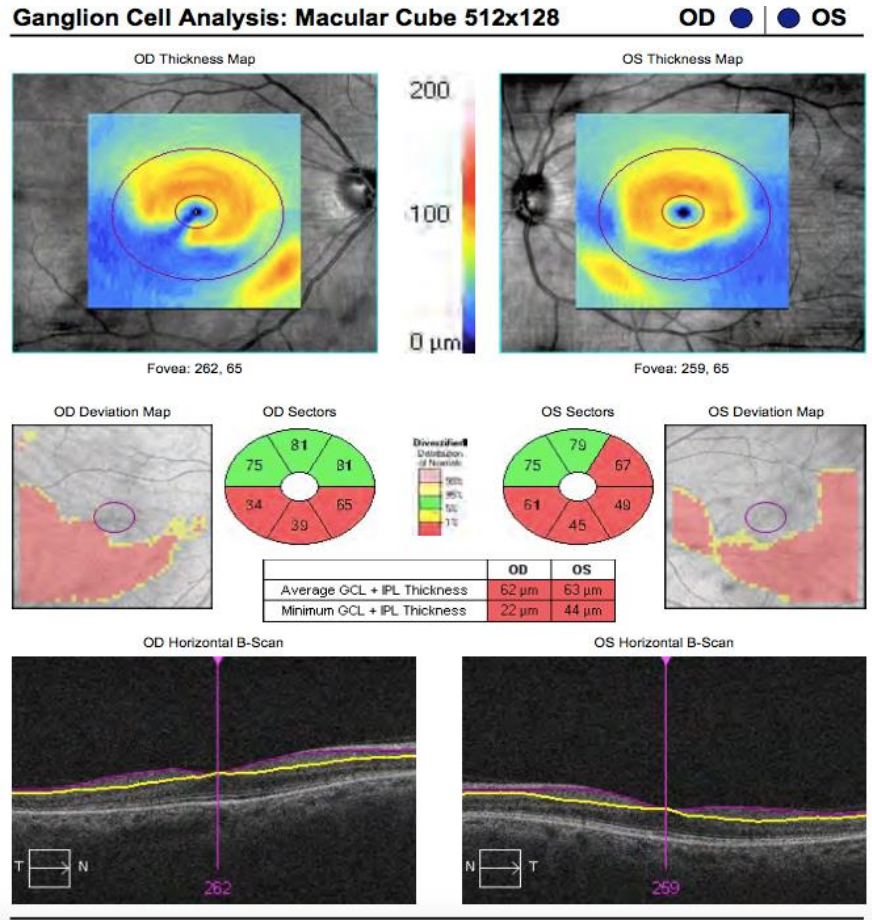
Main Outcome Measures: Sensitivity, specificity, positive likelihood ratio (PLR), and negative likelihood ratio (NLR).

Results: Among GCIPL parameters, the minimum had the best diagnostic performance (sensitivity, 82.0%; specificity, 87.8%; PLR, 6.69; and NLR, 0.21). Inferior quadrant was the best RNFL parameter (sensitivity, 74%; specificity, 95.9%; PLR, 18.13; and NLR, 0.27), as was rim area (sensitivity, 68%; specificity, 98%; PLR, 33.3; and NLR, 0.33) among ONH parameters. The or-logic combination of minimum GCIPL and average RNFL provided the overall best diagnostic performance (sensitivity, 94%; specificity, 85.7%; PRL, 6.58; and NLR, 0.07) as compared with the best RNFL, best ONH, and best and-logic combination (minimum GCIPL and inferior quadrant RNFL; sensitivity, 64%; specificity, 100%; PLR, infinity; and NPR, 0.36).

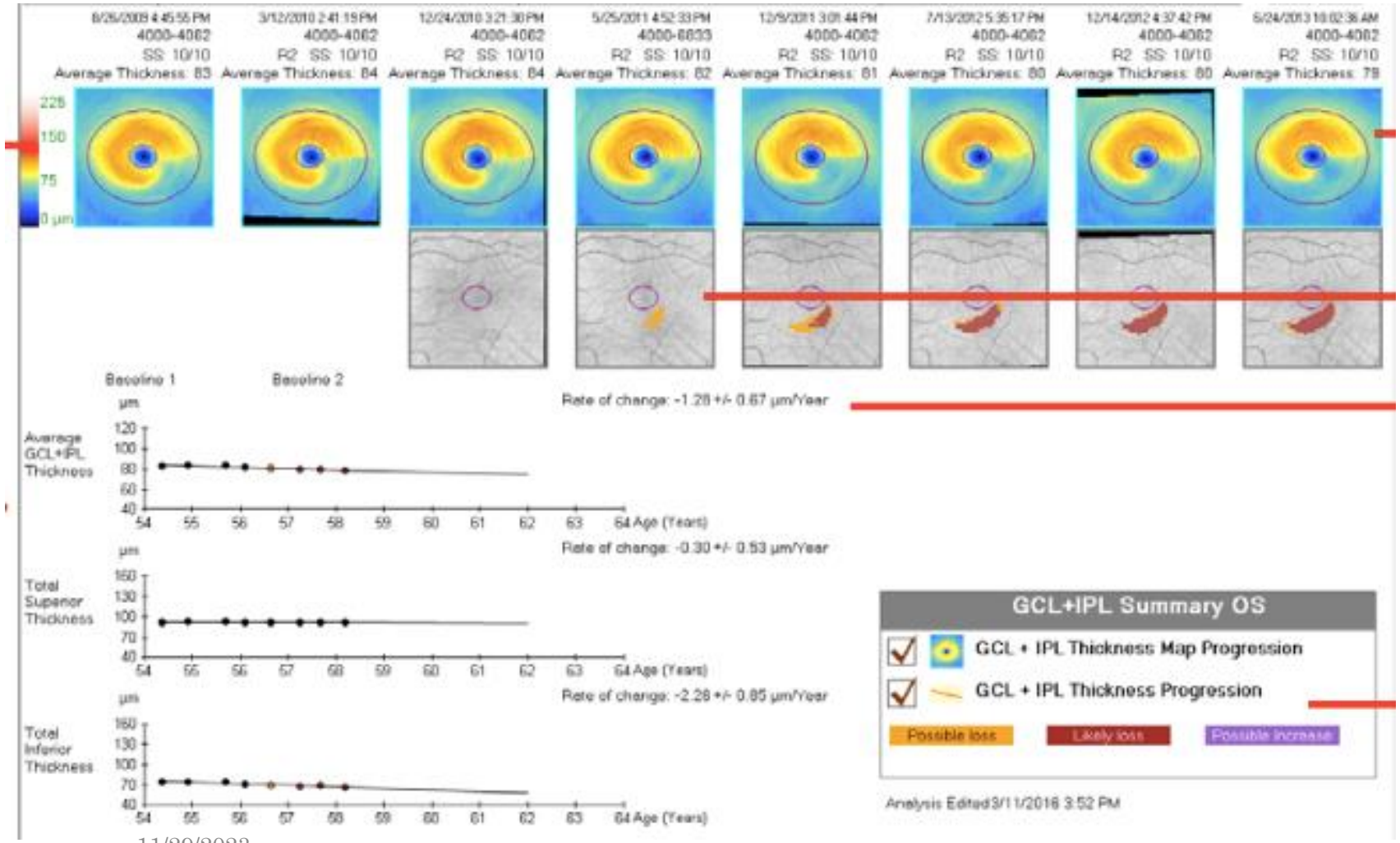
Conclusions: The binary or-logic combination of minimum GCIPL and average RNFL or rim area provides better diagnostic performances than those of and-logic combinations or best single GCIPL, RNFL, or ONH parameters. This finding may be clinically valuable for the diagnosis of early glaucoma. *Ophthalmology 2014;121:849-854 © 2014 by the American Academy of Ophthalmology.*

Ganglion Cell Analysis (GCA)

- **Measures thickness of GCL+IPL**
- **On the Cirrus OCT**
- **GCA algorithm tested only on glaucoma, so watch for any other macular pathology prior to using this scan.**
- **User needs to visually evaluate segmentation, confirm FoveaFinder was successful**

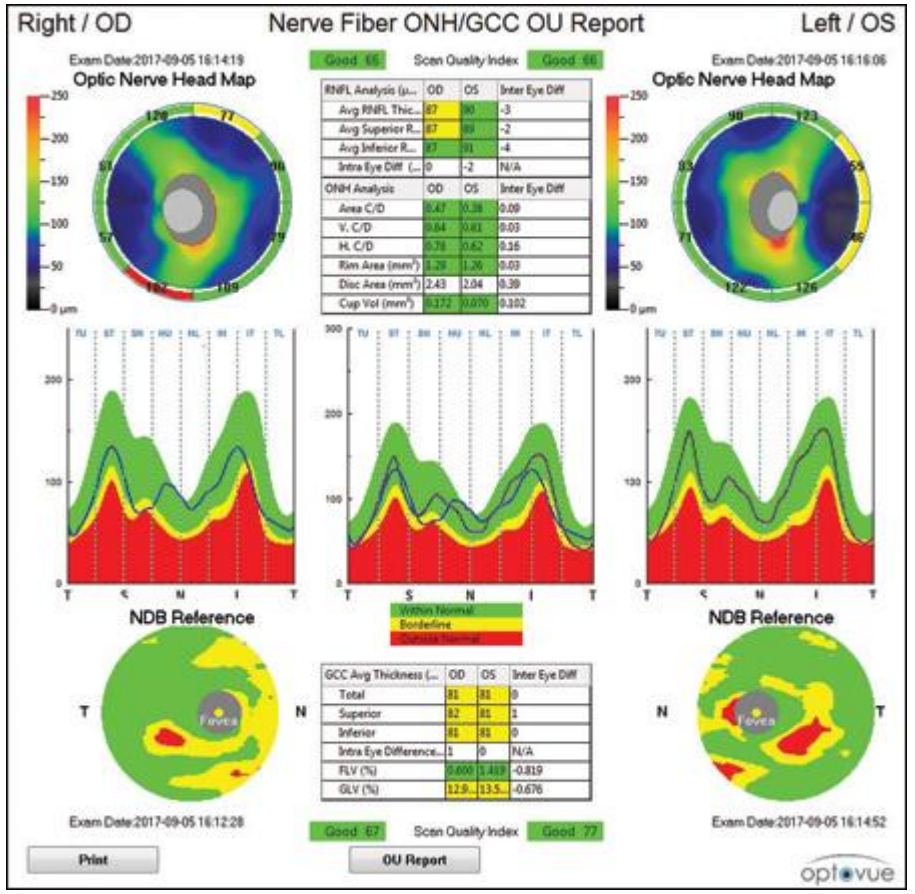


Sample GCA trend analysis



Ganglion Cell Complex (GCC)

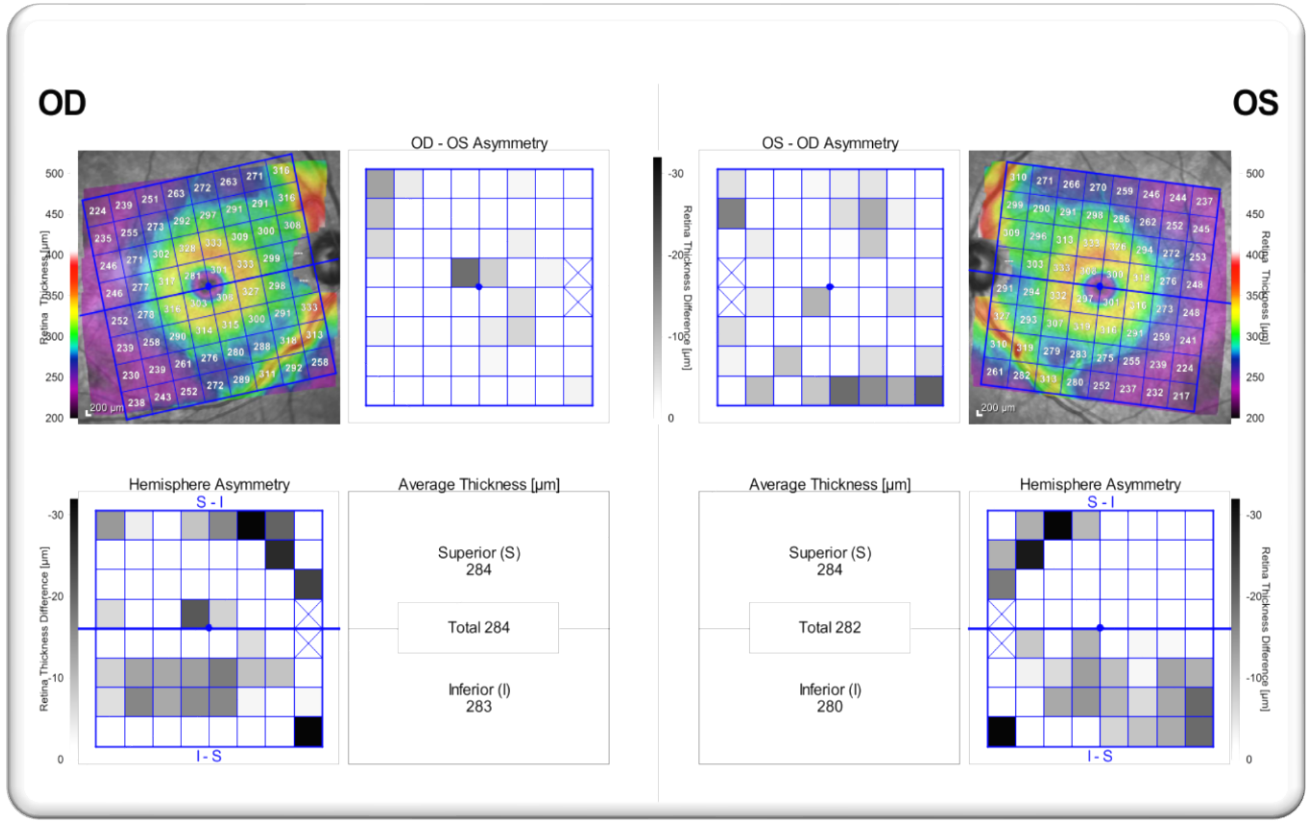
- **Available on the Optovue OCT**
- **In addition to affecting the peripapillary RNFL, Glaucoma preferentially affects the three innermost layers of the retina:**
  - **RNFL**
    - **Contains ganglion cell axons, astrocytes**
  - **Ganglion cell layer**
    - **Contains ganglion cell bodies**
  - **Inner plexiform layer**
    - **Contains Ganglion cell dendrite, bipolar cell axons, amacrine processes.**
  - **These Three layers are called the: <u>Ganglion Cell Complex (GCC)</u>**



https://www.healio.com/news/optometry/20180312/routine-exam-reveals-thinning-gcc

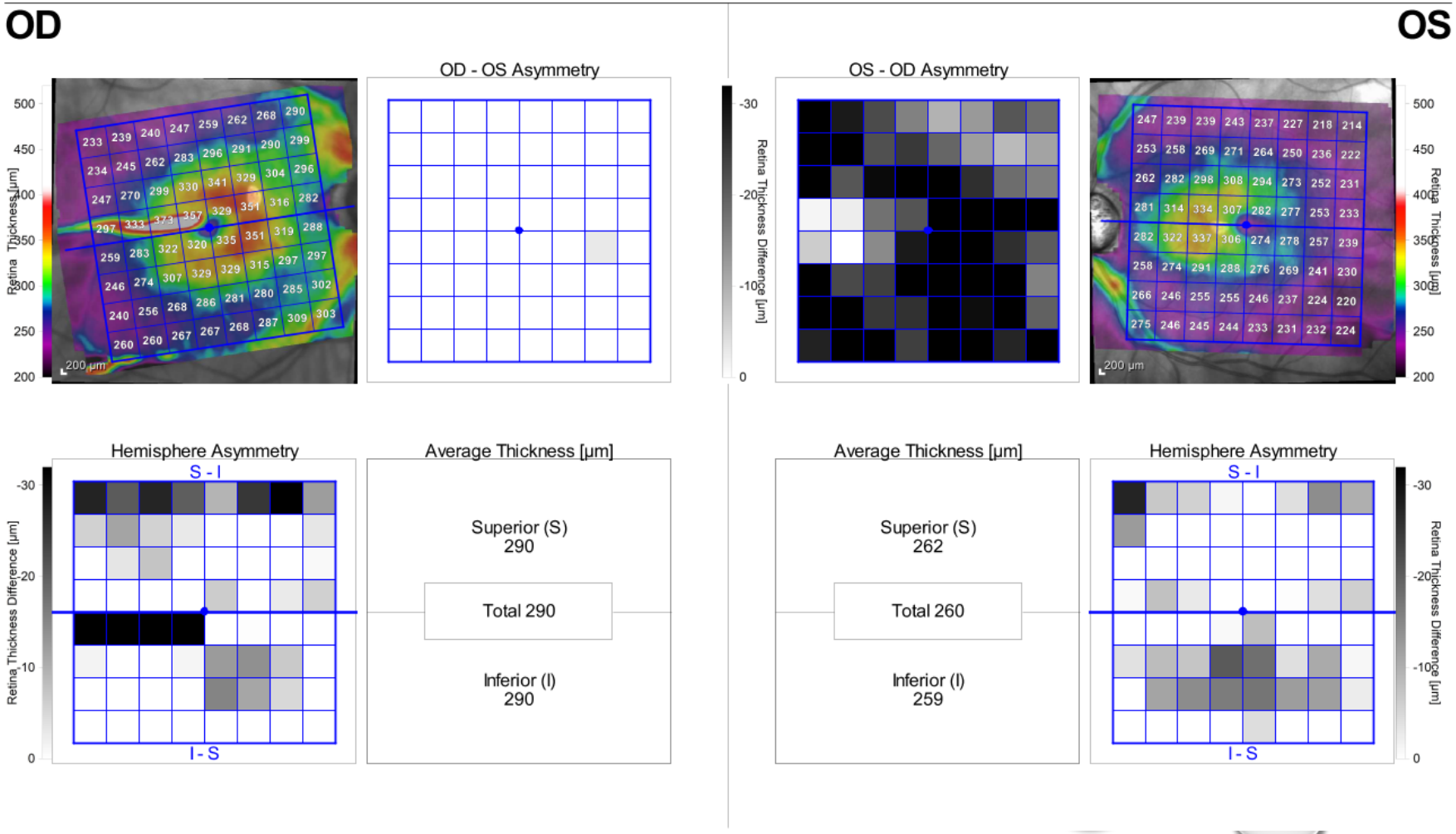
SD

Asymmetry Analysis (Spectralis)

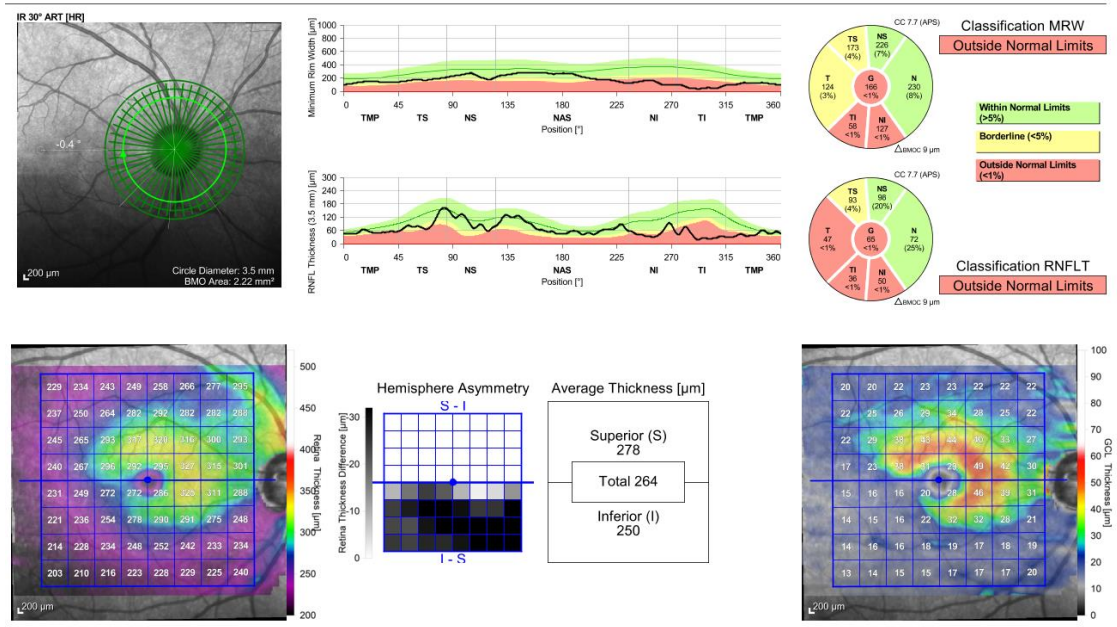


- **Glaucoma is a disease of asymmetry.**
- **This captures the whole retina, so be mindful of artifact**
  - **(ERM, vitreomacular traction, retinal atrophy)**

Asymmetry analysis OS>>OD and artifact OD



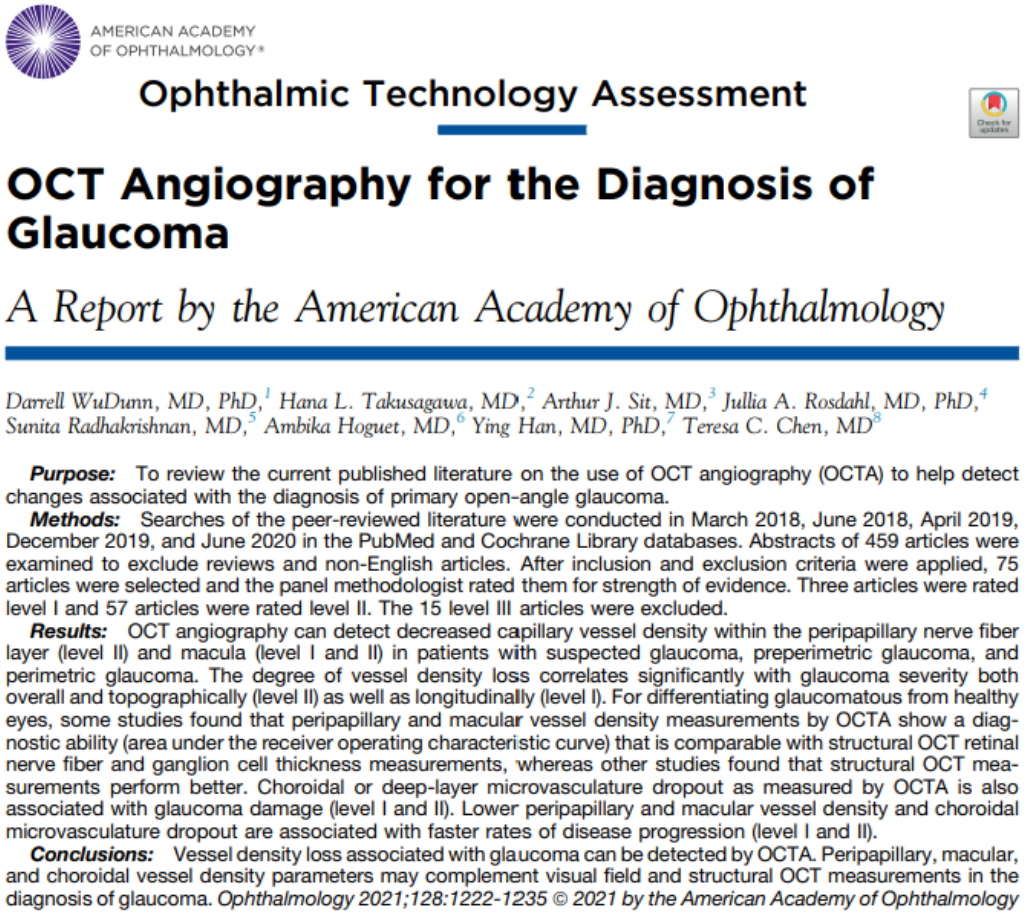
Spectralis Asymmetry/ganglion cell analysis



- Spectralis OCT shows both asymmetry analysis and ganglion cell thickness in its overview slide.

OCT angiography

- **In essentially all studies of OCT angiography and glaucoma to date, the vessel density in the peripapillary region is decreased in eye with glaucoma compared to healthy eyes.**
- **Most studies have shown a correlation between the degree of vessel loss and the severity of the patient's glaucoma.**



AMERICAN ACADEMY OF OPHTHALMOLOGY®

Ophthalmic Technology Assessment

OCT Angiography for the Diagnosis of Glaucoma

A Report by the American Academy of Ophthalmology

Darrell WuDunn, MD, PhD,[1] Hana L. Takusagawa, MD,[2] Arthur J. Sit, MD,[3] Jullia A. Rosdahl, MD, PhD,[4] Sunita Radhakrishnan, MD,[5] Ambika Hoguet, MD,[6] Ying Han, MD, PhD,[7] Teresa C. Chen, MD[8]

Purpose: To review the current published literature on the use of OCT angiography (OCTA) to help detect changes associated with the diagnosis of primary open-angle glaucoma.

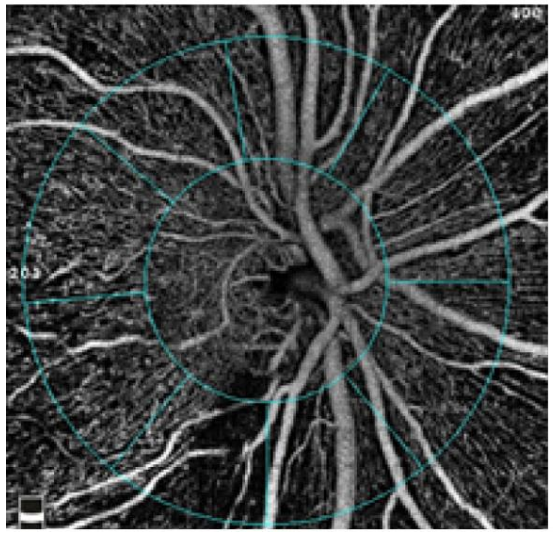
Methods: Searches of the peer-reviewed literature were conducted in March 2018, June 2018, April 2019, December 2019, and June 2020 in the PubMed and Cochrane Library databases. Abstracts of 459 articles were examined to exclude reviews and non-English articles. After inclusion and exclusion criteria were applied, 75 articles were selected and the panel methodologist rated them for strength of evidence. Three articles were rated level I and 57 articles were rated level II. The 15 level III articles were excluded.

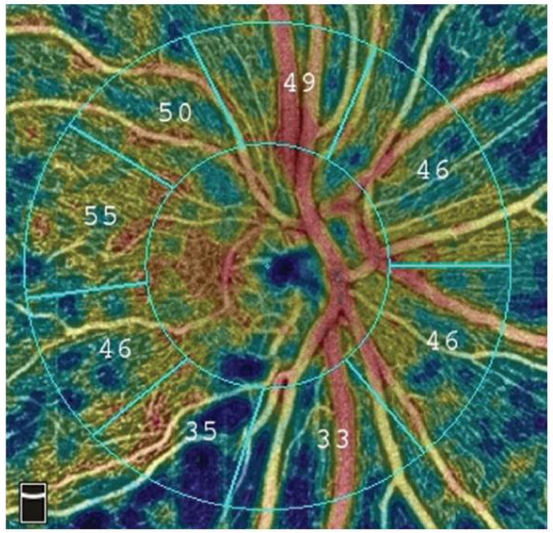
Results: OCT angiography can detect decreased capillary vessel density within the peripapillary nerve fiber layer (level II) and macula (level I and II) in patients with suspected glaucoma, preperimetric glaucoma, and perimetric glaucoma. The degree of vessel density loss correlates significantly with glaucoma severity both overall and topographically (level II) as well as longitudinally (level I). For differentiating glaucomatous from healthy eyes, some studies found that peripapillary and macular vessel density measurements by OCTA show a diagnostic ability (area under the receiver operating characteristic curve) that is comparable with structural OCT retinal nerve fiber and ganglion cell thickness measurements, whereas other studies found that structural OCT measurements perform better. Choroidal or deep-layer microvasculature dropout as measured by OCTA is also associated with glaucoma damage (level I and II). Lower peripapillary and macular vessel density and choroidal microvasculature dropout are associated with faster rates of disease progression (level I and II).

Conclusions: Vessel density loss associated with glaucoma can be detected by OCTA. Peripapillary, macular, and choroidal vessel density parameters may complement visual field and structural OCT measurements in the diagnosis of glaucoma. *Ophthalmology 2021;128:1222-1235*

OCT angiography and glaucoma.

- **In this study for glaucomatous eyes, the association of RNFL thickness and capillary density was strong. The association was strongest in the IT region.**





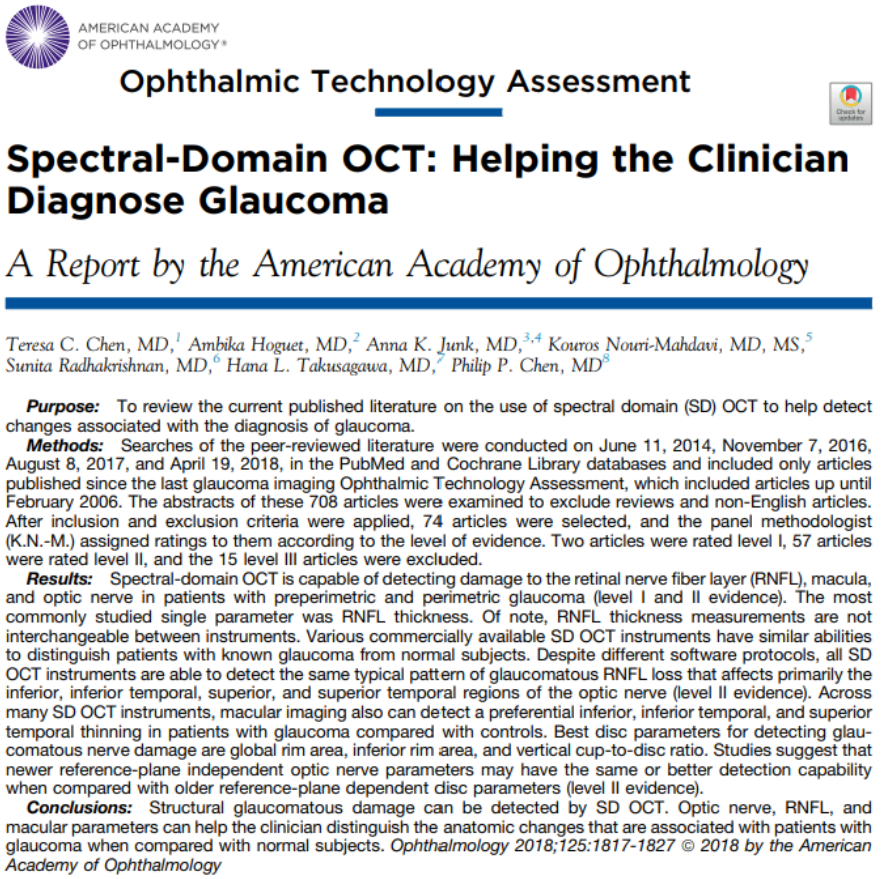
https://www.reviewofoptometry.com/article/adding-octa-increases-diagnostic-sensitivity-in-glaucoma

Measurements of OCTA Complement OCT for Diagnosing Early Primary Open Angle Glaucoma
Ophthalmol Glaucoma. 2022 ; 5(3): 262–274. doi:10.1016/j.ogla.2021.09.012

Question Two: Is the information I received from my OCT reliable and what artifacts should I be looking for?

Points to consider:

1. **Reliability of the image**
   - Garbage in/garbage out
2. **Variability of the RNFL scan**
   - Is the change significant?
3. **Segmentation of the images**
   - Even if the reliability is acceptable, was the image captured correctly?



AMERICAN ACADEMY OF OPHTHALMOLOGY®

Ophthalmic Technology Assessment

Spectral-Domain OCT: Helping the Clinician Diagnose Glaucoma

A Report by the American Academy of Ophthalmology

Teresa C. Chen, MD,[1] Ambika Hoguet, MD,[2] Anna K. Junk, MD,[3,4] Kouros Nouri-Mahdavi, MD, MS,[5] Sunita Radhakrishnan, MD,[6] Hana L. Takusagawa, MD,[7] Philip P. Chen, MD[8]

Purpose: To review the current published literature on the use of spectral domain (SD) OCT to help detect changes associated with the diagnosis of glaucoma.

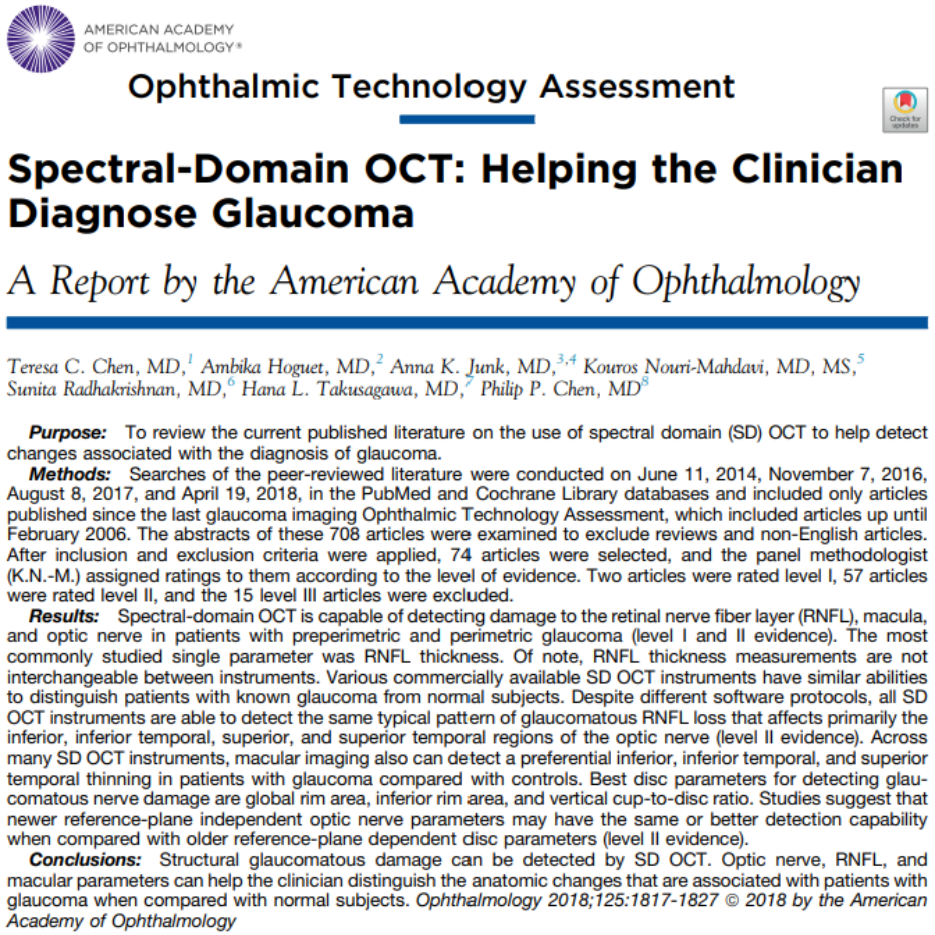
Methods: Searches of the peer-reviewed literature were conducted on June 11, 2014, November 7, 2016, August 8, 2017, and April 19, 2018, in the PubMed and Cochrane Library databases and included only articles published since the last glaucoma imaging Ophthalmic Technology Assessment, which included articles up until February 2006. The abstracts of these 708 articles were examined to exclude reviews and non-English articles. After inclusion and exclusion criteria were applied, 74 articles were selected, and the panel methodologist (K.N.-M.) assigned ratings to them according to the level of evidence. Two articles were rated level I, 57 articles were rated level II, and the 15 level III articles were excluded.

Results: Spectral-domain OCT is capable of detecting damage to the retinal nerve fiber layer (RNFL), macula, and optic nerve in patients with preperimetric and perimetric glaucoma (level I and II evidence). The most commonly studied single parameter was RNFL thickness. Of note, RNFL thickness measurements are not interchangeable between instruments. Various commercially available SD OCT instruments have similar abilities to distinguish patients with known glaucoma from normal subjects. Despite different software protocols, all SD OCT instruments are able to detect the same typical pattern of glaucomatous RNFL loss that affects primarily the inferior, inferior temporal, superior, and superior temporal regions of the optic nerve (level II evidence). Across many SD OCT instruments, macular imaging also can detect a preferential inferior, inferior temporal, and superior temporal thinning in patients with glaucoma compared with controls. Best disc parameters for detecting glaucomatous nerve damage are global rim area, inferior rim area, and vertical cup-to-disc ratio. Studies suggest that newer reference-plane independent optic nerve parameters may have the same or better detection capability when compared with older reference-plane dependent disc parameters (level II evidence).

Conclusions: Structural glaucomatous damage can be detected by SD OCT. Optic nerve, RNFL, and macular parameters can help the clinician distinguish the anatomic changes that are associated with patients with glaucoma when compared with normal subjects. *Ophthalmology 2018;125:1817-1827 © 2018 by the American Academy of Ophthalmology*

Reliability/resolution of scans

- **Cirrus:**
  - **Reliability: signal strength at least 6**
  - **Axial resolution: 5 um**
- **RTVue:**
  - **Reliability: signal strength at least 30 or 45 (depending on the study)**
  - **Axial resolution: 5 um**
- **Spectralis:**
  - **Reliability: at least 15 (I use 20)**
  - **Axial resolution: 7 um**



AMERICAN ACADEMY OF OPHTHALMOLOGY®

Ophthalmic Technology Assessment

Spectral-Domain OCT: Helping the Clinician Diagnose Glaucoma

A Report by the American Academy of Ophthalmology

Teresa C. Chen, MD,[1] Ambika Hoguet, MD,[2] Anna K. Junk, MD,[3,4] Kouros Nouri-Mahdavi, MD, MS,[5] Sunita Radhakrishnan, MD,[6] Hana L. Takusagawa, MD,[7] Philip P. Chen, MD[8]

Purpose: To review the current published literature on the use of spectral domain (SD) OCT to help detect changes associated with the diagnosis of glaucoma.

Methods: Searches of the peer-reviewed literature were conducted on June 11, 2014, November 7, 2016, August 8, 2017, and April 19, 2018, in the PubMed and Cochrane Library databases and included only articles published since the last glaucoma imaging Ophthalmic Technology Assessment, which included articles up until February 2006. The abstracts of these 708 articles were examined to exclude reviews and non-English articles. After inclusion and exclusion criteria were applied, 74 articles were selected, and the panel methodologist (K.N.-M.) assigned ratings to them according to the level of evidence. Two articles were rated level I, 57 articles were rated level II, and the 15 level III articles were excluded.

Results: Spectral-domain OCT is capable of detecting damage to the retinal nerve fiber layer (RNFL), macula, and optic nerve in patients with preperimetric and perimetric glaucoma (level I and II evidence). The most commonly studied single parameter was RNFL thickness. Of note, RNFL thickness measurements are not interchangeable between instruments. Various commercially available SD OCT instruments have similar abilities to distinguish patients with known glaucoma from normal subjects. Despite different software protocols, all SD OCT instruments are able to detect the same typical pattern of glaucomatous RNFL loss that affects primarily the inferior, inferior temporal, superior, and superior temporal regions of the optic nerve (level II evidence). Across many SD OCT instruments, macular imaging also can detect a preferential inferior, inferior temporal, and superior temporal thinning in patients with glaucoma compared with controls. Best disc parameters for detecting glaucomatous nerve damage are global rim area, inferior rim area, and vertical cup-to-disc ratio. Studies suggest that newer reference-plane independent optic nerve parameters may have the same or better detection capability when compared with older reference-plane dependent disc parameters (level II evidence).

Conclusions: Structural glaucomatous damage can be detected by SD OCT. Optic nerve, RNFL, and macular parameters can help the clinician distinguish the anatomic changes that are associated with patients with glaucoma when compared with normal subjects. *Ophthalmology 2018;125:1817-1827*

Possible artifacts on OCT RNFL

- **Review of 2313 scans on Spectralis**
- **Decentration error in 27.8% or all artifacts (may have improved with BMO-MRA update)**
- **Posterior vitreous detachment artifacts in 14.4%**

<u>Other factors associated with artifacts:</u>

1. **Visual acuity less than 20/40**
2. **Moderate to severe cataracts**
3. **Advanced glaucoma**

Published in final edited form as:
Am J Ophthalmol. 2015 March ; 159(3): 565–76.e2. doi:10.1016/j.ajo.2014.12.006.

Patient Characteristics Associated with Artifacts in Spectralis Optical Coherence Tomography Imaging of the Retinal Nerve Fiber Layer in Glaucoma

Yingna Liu, BA[1], **Huseyin Simavli, MD**[1,2], **Christian Que, MD**[1,2], **Jennifer L. Rizzo, MD**[2], **Edem Tsikata, PhD**[1,2], **Rie Maurer, MA**[1,3], and **Teresa Chen, MD**[1,2]

[1]Harvard Medical School, Boston, MA

[2]Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, MA

[3]Center for Clinical Investigation, Brigham and Women's Hospital, Boston, MA

Abstract

Purpose—To determine patient factors and eye conditions associated with artifacts in Spectralis optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) scans.

Design—Retrospective cross-sectional study.

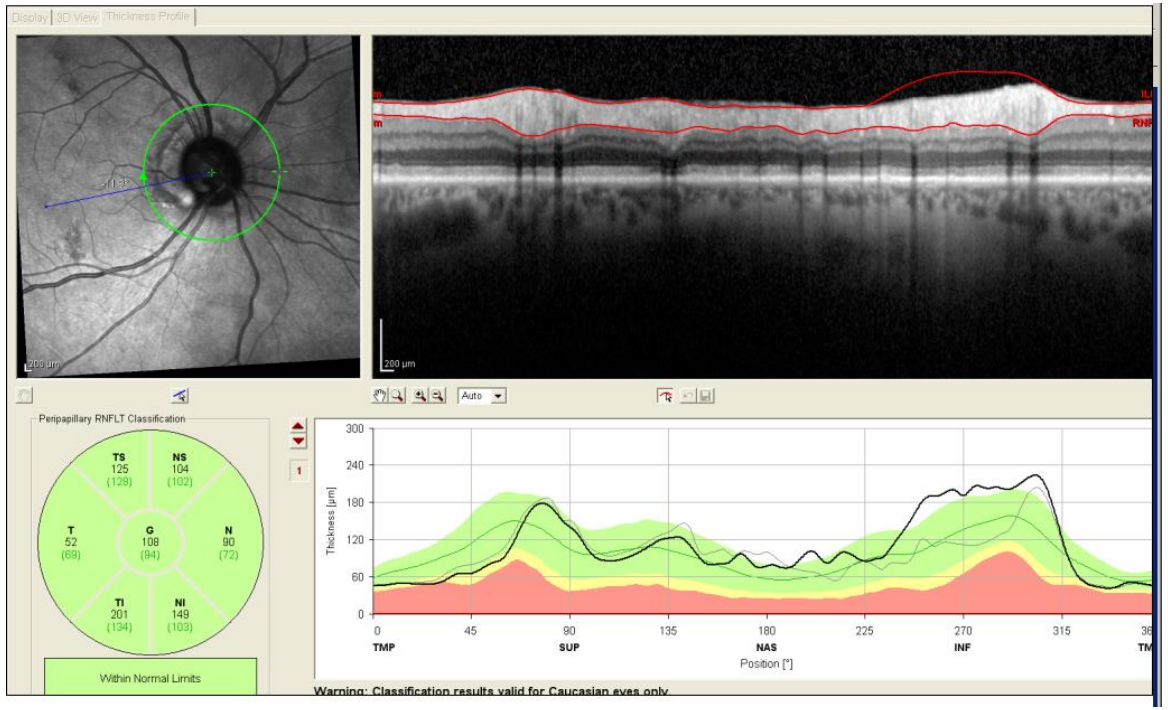
Methods—The prevalence of twelve artifact types were described in this review of 2313 eye scans from 1188 patients who underwent a complete eye exam with Spectralis OCT scanning during the period of September 2009 to July 2013. Generalized estimating equations model was utilized to analyze associations between increased artifact prevalence and 10 patient characteristics, which included age, sex, race, visual acuity, refractive error, astigmatism, cataract status, glaucoma staging, visual field reliability, and glaucoma diagnosis.

Results—A total of 1070 or 46.3% of the 2313 eye scans had at least one artifact. De-centration error was the most common artifact (27.8%), followed by posterior vitreous detachment artifacts (14.4%). Visual acuity of less than 20/40 ($p<0.0001$), presence of moderate to severe cataracts ($p<0.0001$), advanced stage of glaucoma ($p<0.0001$), and a diagnosis of open angle glaucoma ($p=0.0003$) were associated with increased prevalence of artifacts.

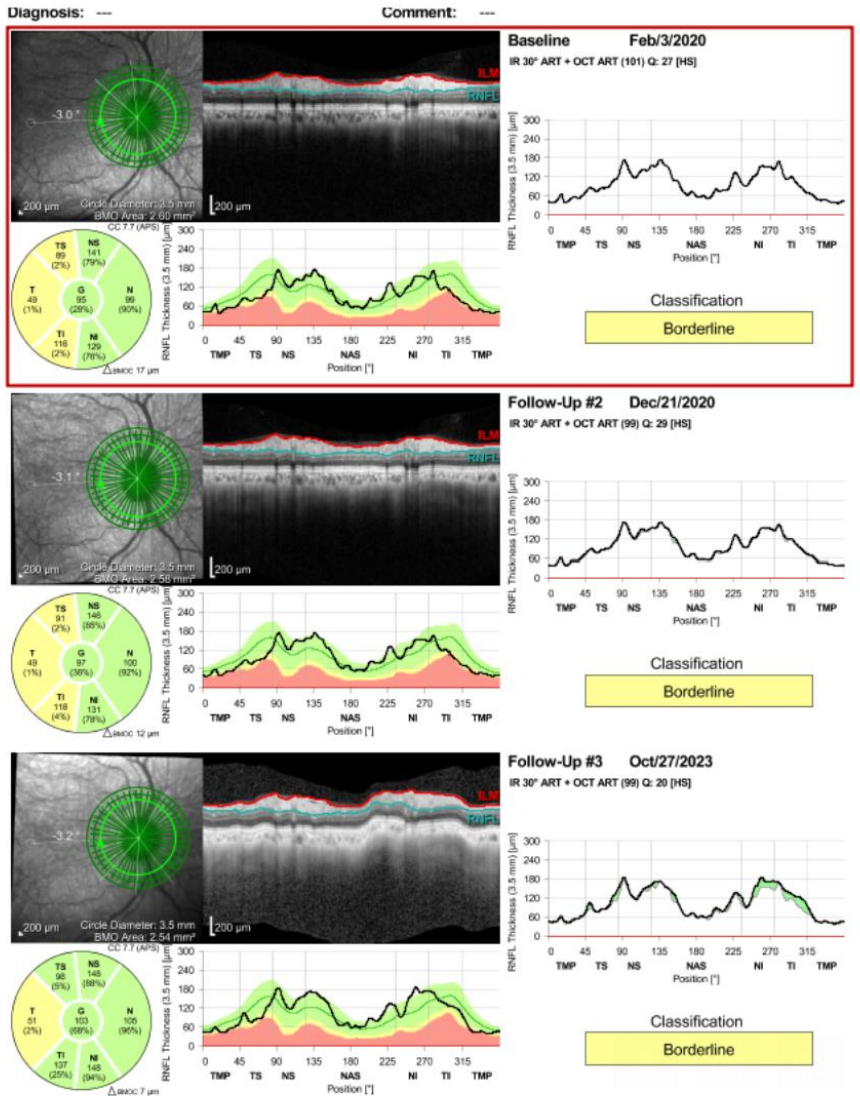
Conclusions—Clinicians should first assess scans for artifacts before making therapeutic decisions based on RNFL thickness measurements.

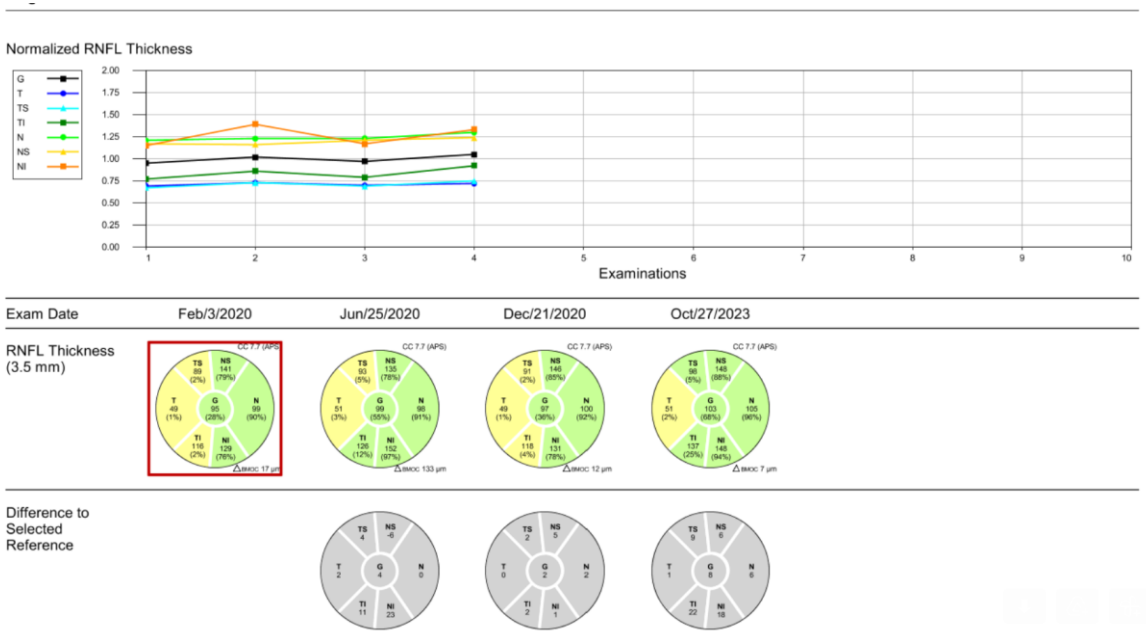
Abnormal segmentation

- **<u>ALWAYS</u> look at the cross section of the RNFL to make sure the RNFL was acquired without scanning errors.**
- **This will NOT be caught by the image reliability.**
- **In this example, the RNFL looks especially thick in the inferotemporal and inferonasal quadrants because of an error in the scan**



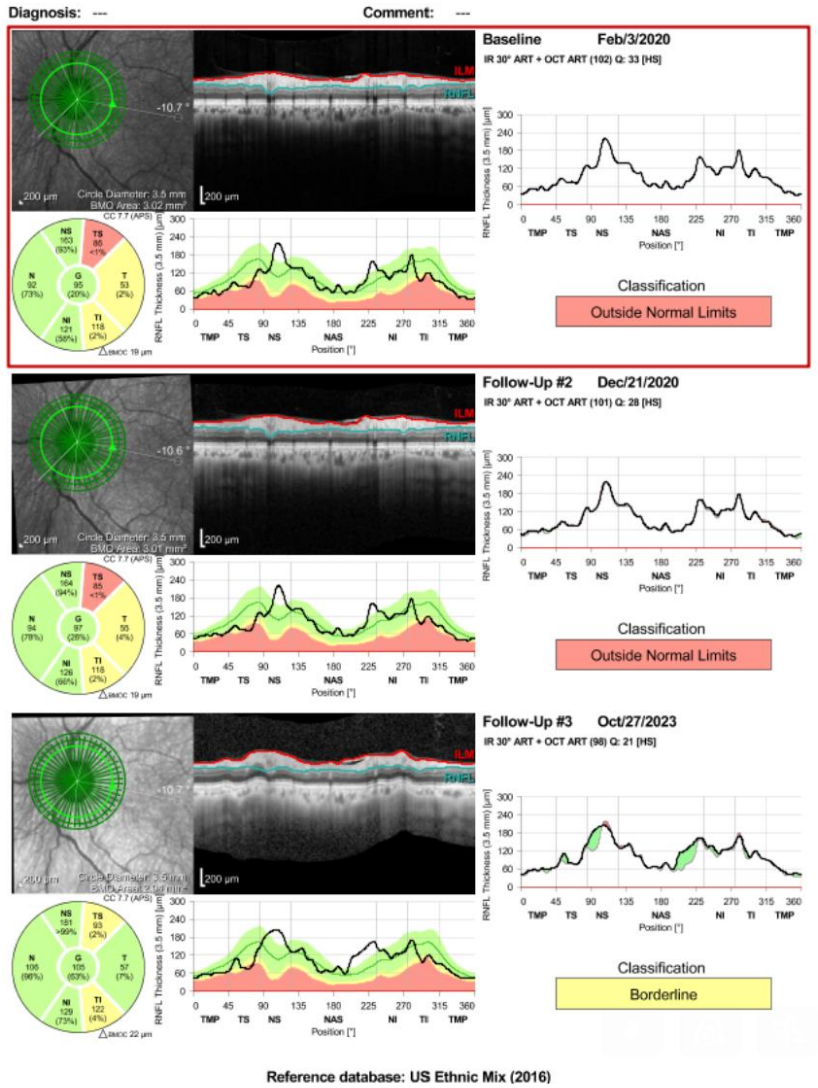
Poor image quality

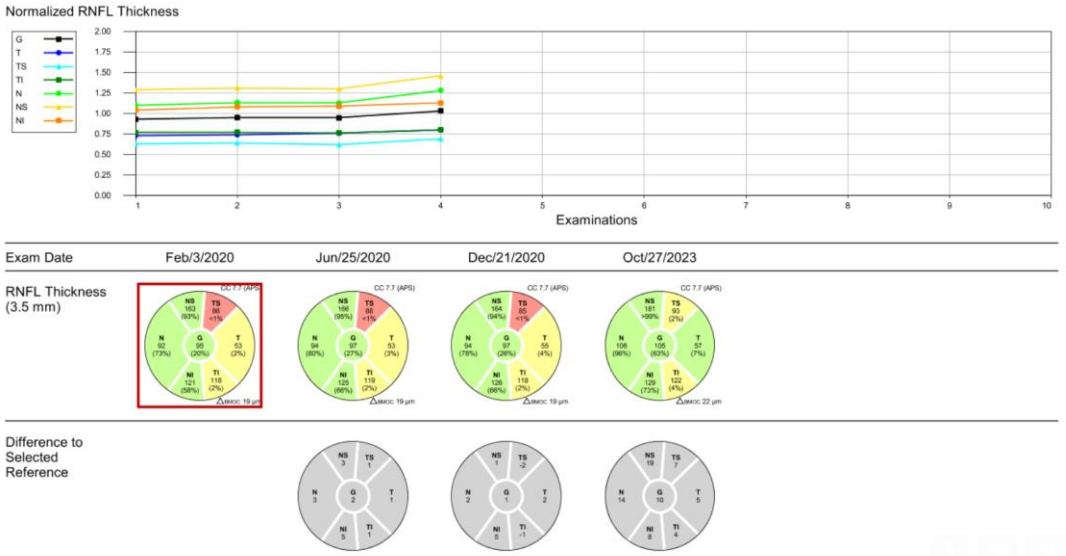




Because the image quality was poor, the RNFL is THICKER on the October 2023 scan. This can be seen easily on the cross section of the RNFL.

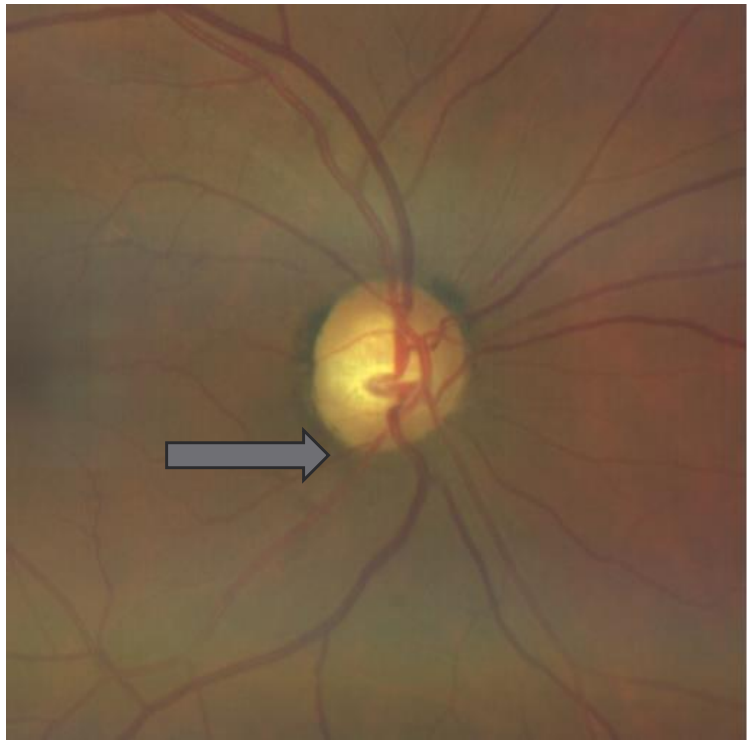
Poor image quality



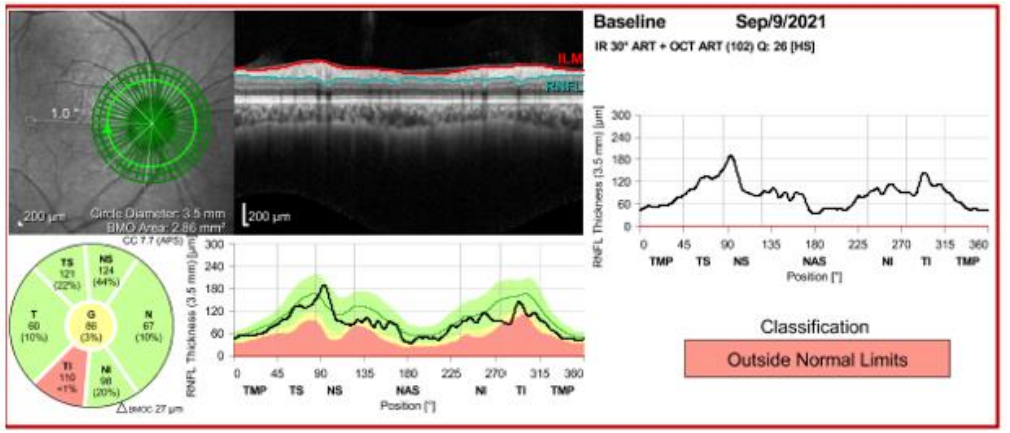


Exactly the same issue is seen with the fellow eye.

Question three: Does the OCT data correlate with my clinical interpretation of the optic nerve and the patient's visual field?

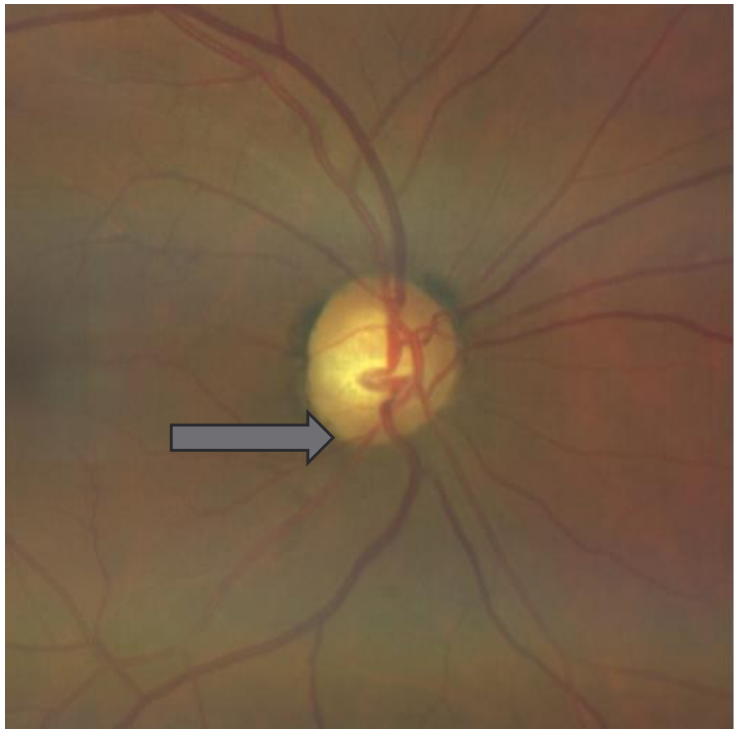


Clinically, the ONH looks thinner inferiorly

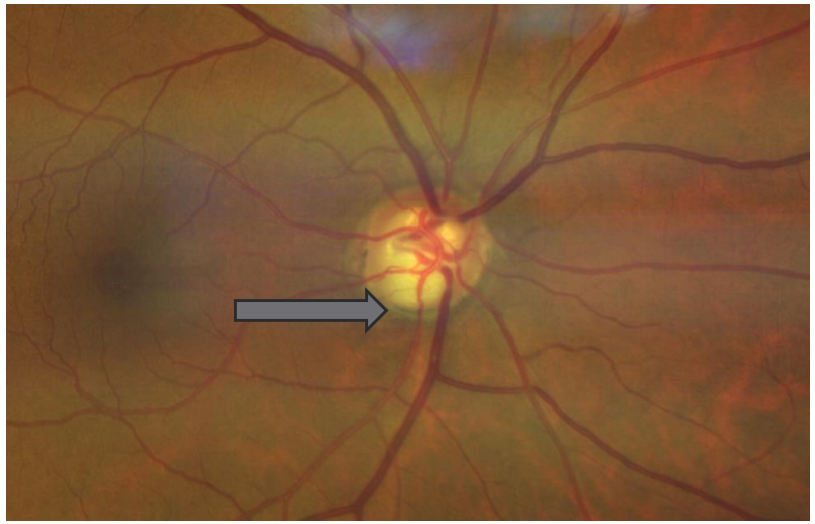


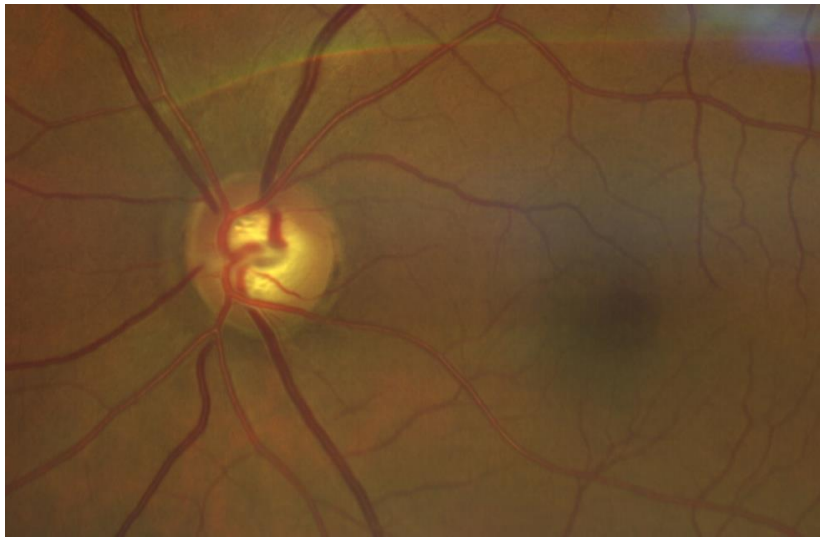
Does the OCT data correlate with my clinical interpretation of the optic nerve and the patient's visual field?

- If the OCT NFL does not match clinical interpretation or the visual field, make sure to review all the information provided by the OCT and not just the OCT RNFL
- You may be missing important information



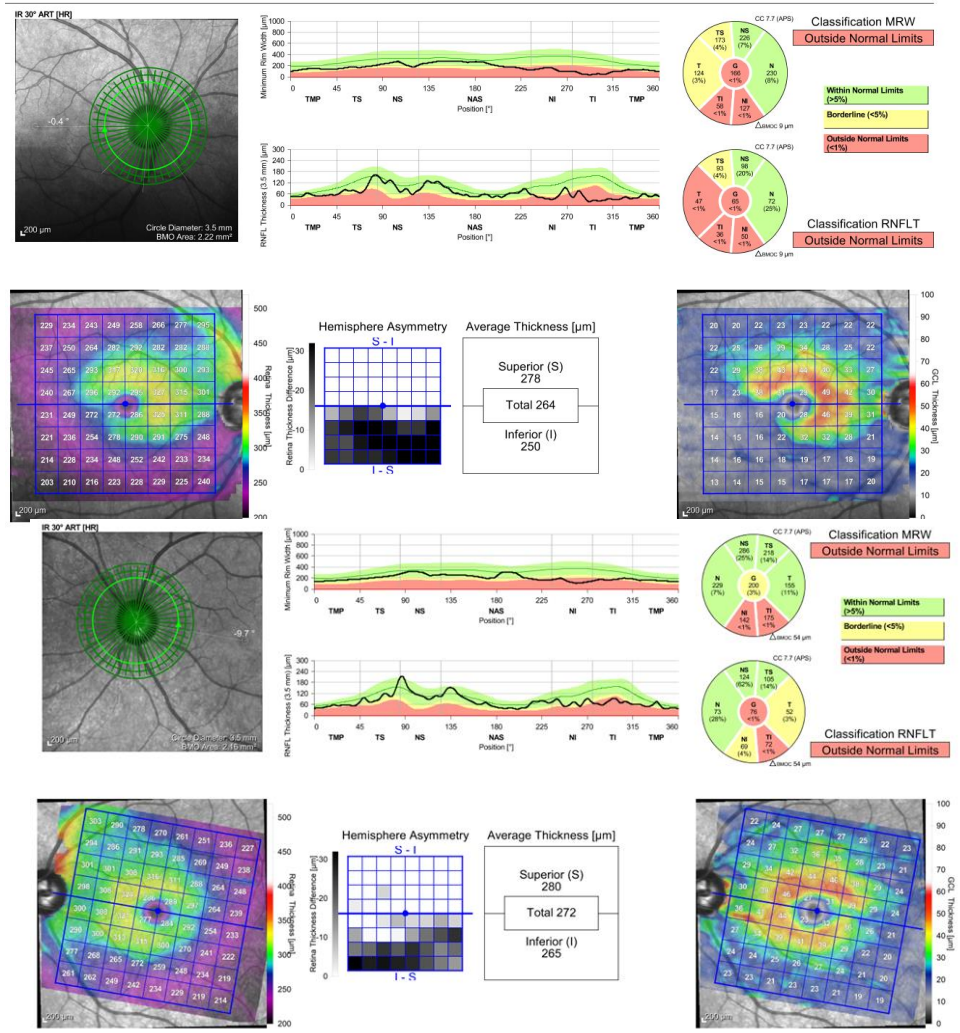
Excellent correlation between OCT RNFL, ONHs and VFs





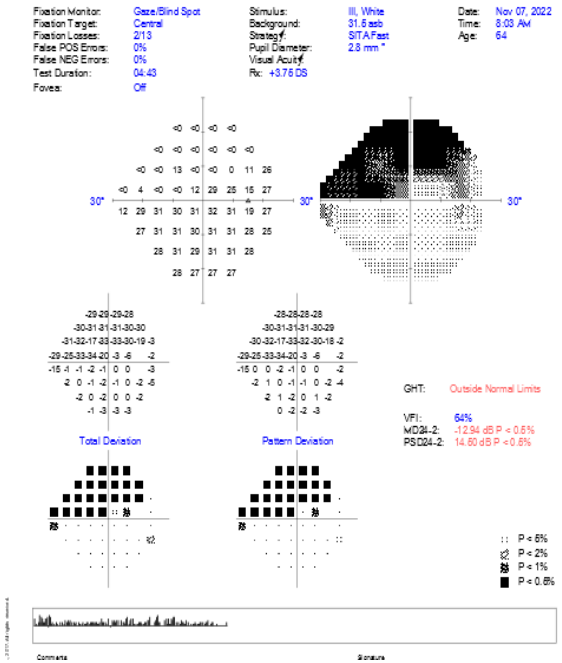
- 65 year old AA male.
- Wants to get medications for his glaucoma through the VA.
- Medications: latanoprost qhs OU, dorzolamide BID OU
- BCVA 20/20 OD/OS
- IOP: 17 mmHG OU
- PACH: 626/630
- ONH:
  - OD: 0.80 c/d, minimal inferior rim
  - OS: 0.60 c/d, thinner inferiorly

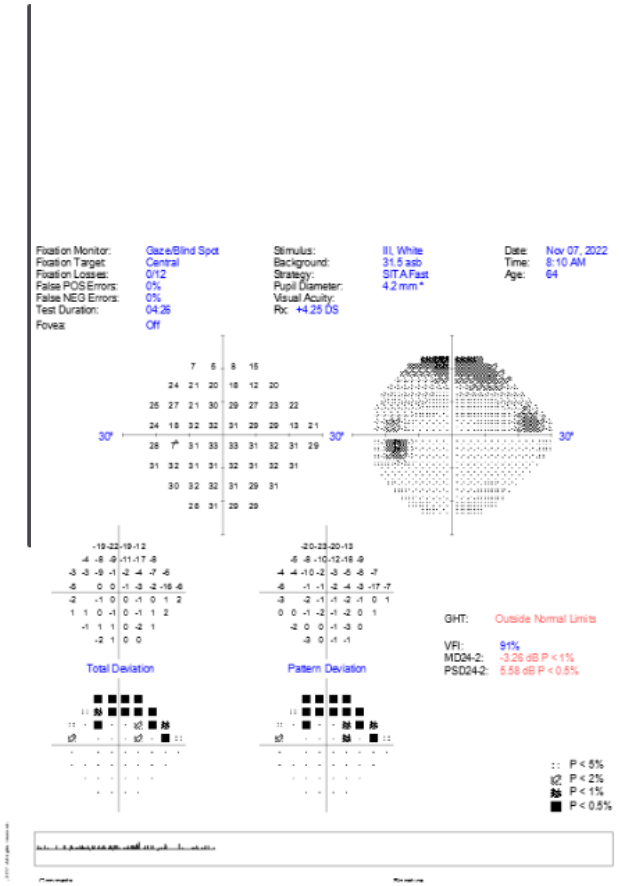
OCT RNFL



- OCT RNFL scans match perfectly with the Clinical ONH appearance and show significant loss of RNFL inferiorly OU (OD>>OS)
- This also correlates well with the asymmetry analysis, OCT ONH analysis and ganglion cell analysis

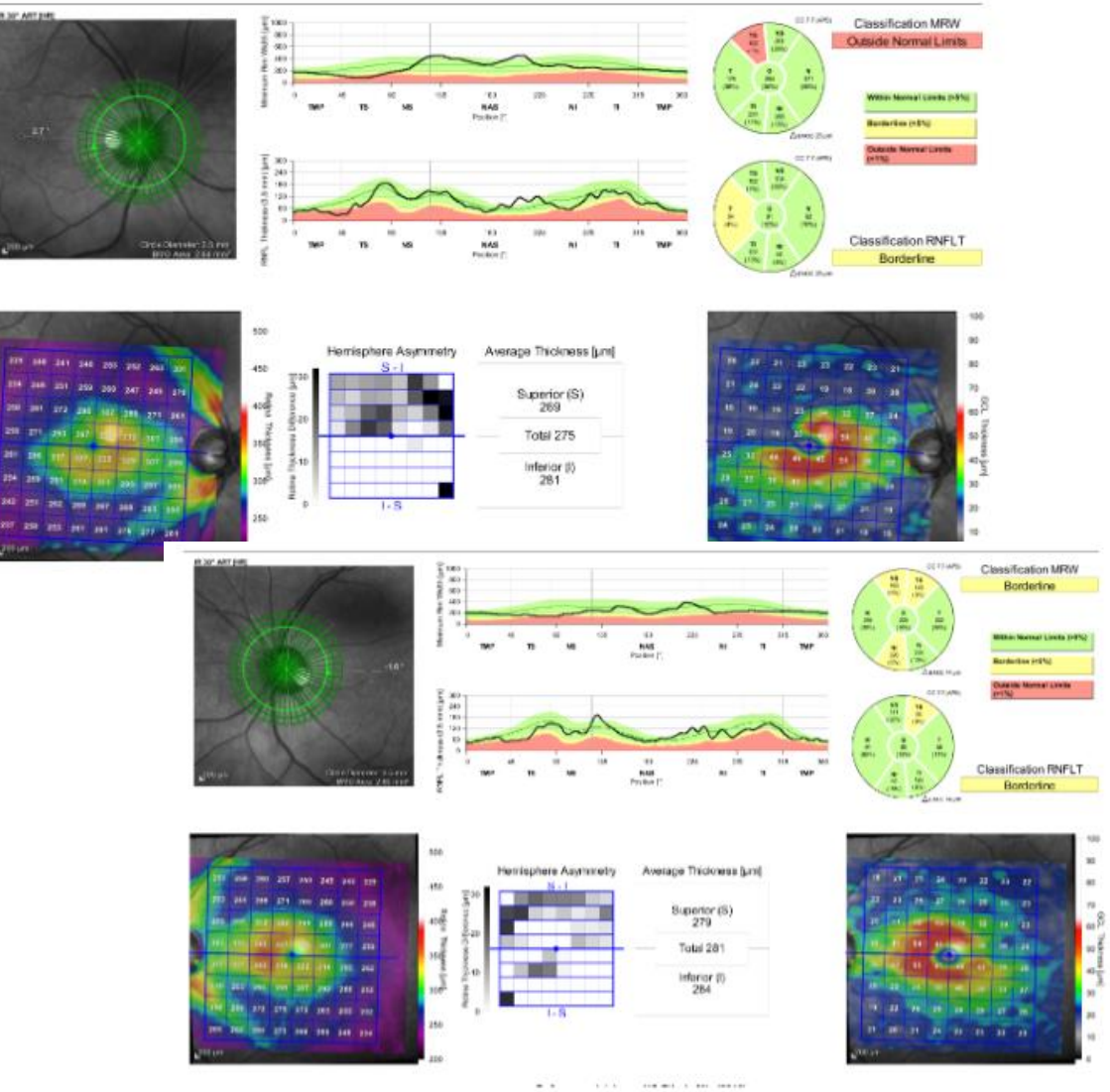
Visual Fields





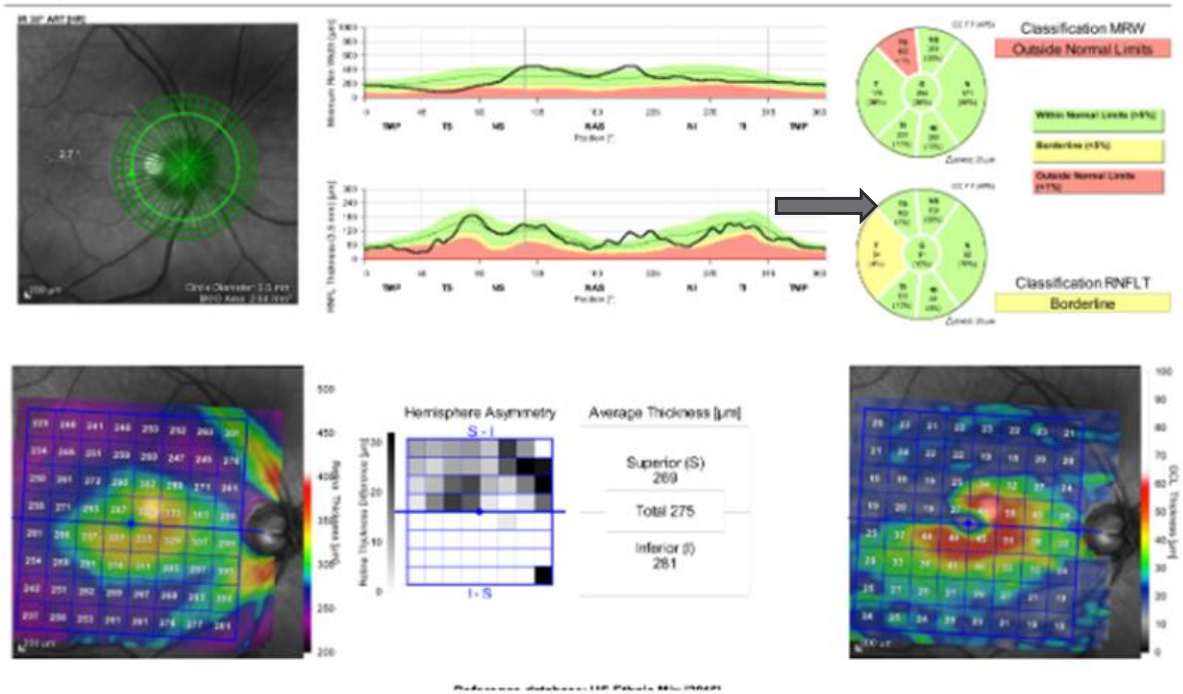
- Excellent correlation between ONH appearance, OCT RNFL/ganglion cell analysis and visual fields in this patient.

Poor correlation between OCT RNFL, Ganglion cells and VFs



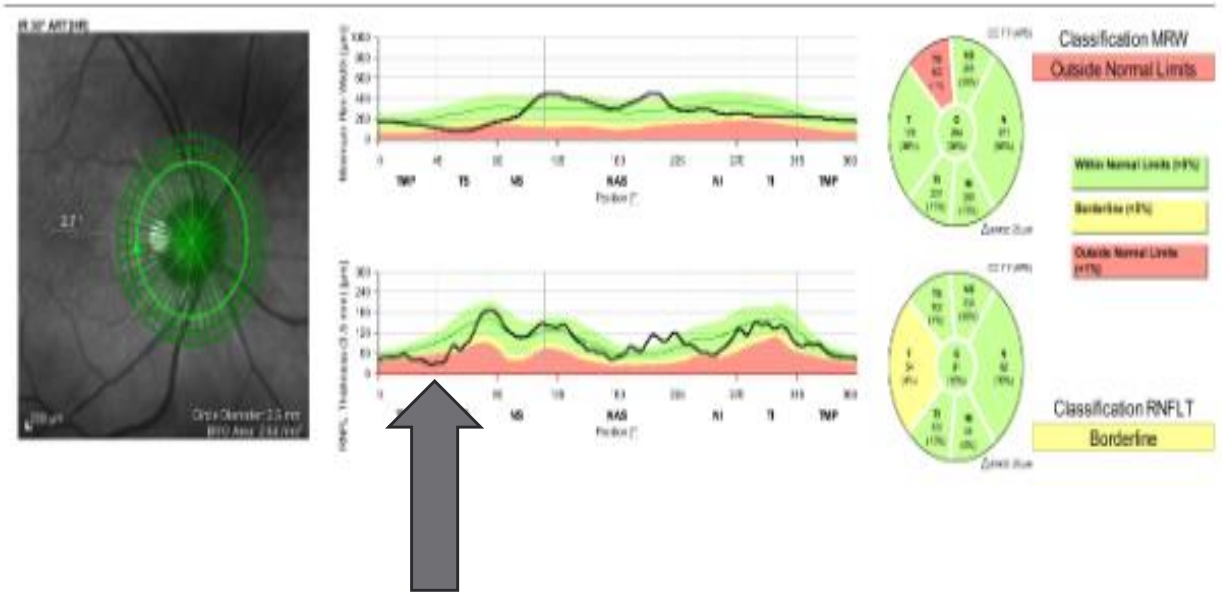
- 68 yo white male
- 1st eye exam in 8 years
- VA sc:
  - OD: 20/20
  - OS: 20/20
  - ONH:
    - OD: 0.60, thinner superiorly
    - OS: 0.65, thinner superiorly

Poor correlation between OCT RNFL, Ganglion cells and VFs



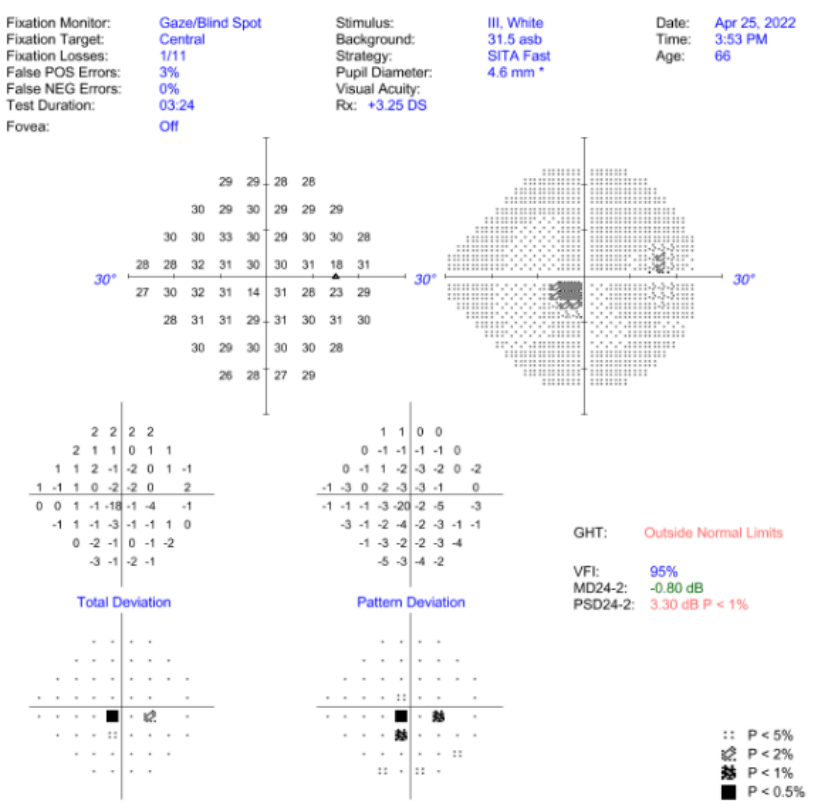
- Looking at the OCT, the ONH is flagged as thin superior temporally which correlates to clinical impression
- The asymmetry analysis and ganglion cell analysis are thinner superiorly
- The OCT RNFL is WNL superior temporally……why?

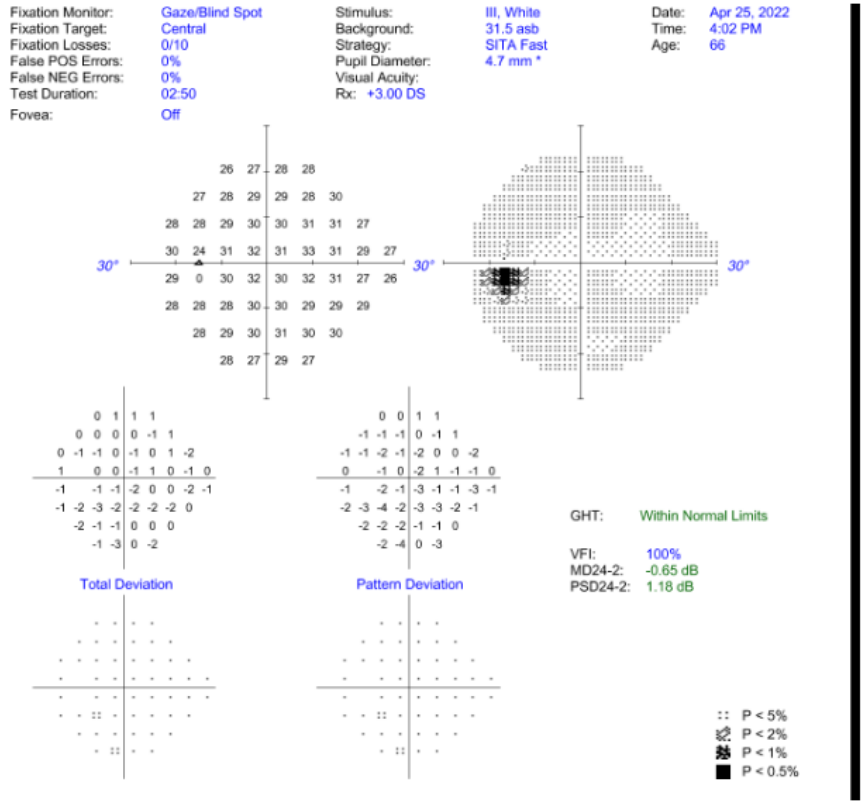
Looking closer at the RNFL



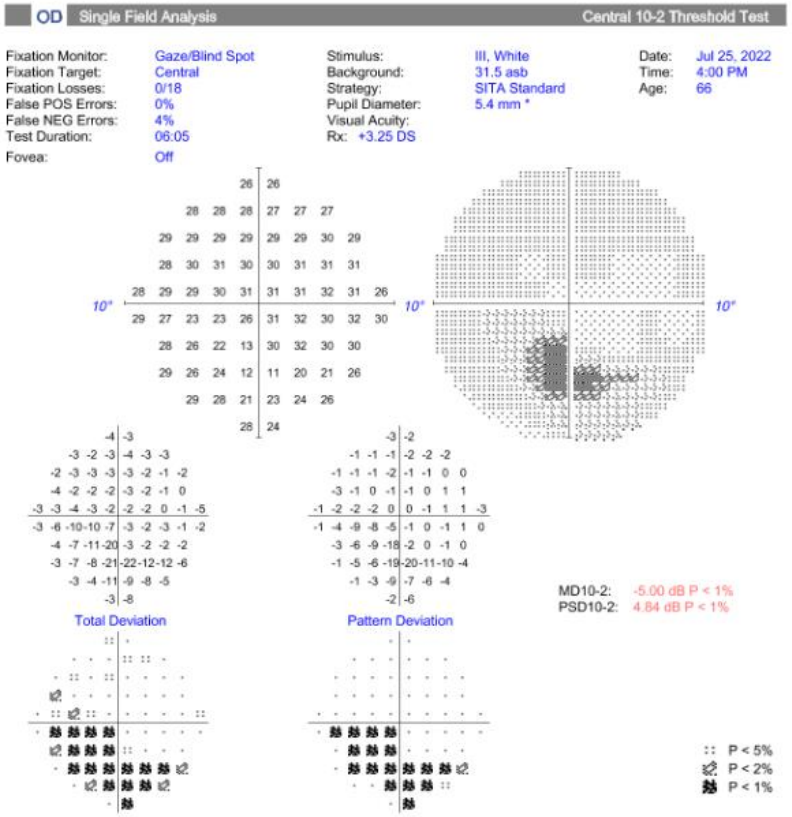
- If you look at the cross-section of the RNFL superior temporally, it dips significantly into the ONL area, but the wedge is an average of the RNFL in that area and shows up WNL because the remaining RNFL superior temporally is plentiful.
- This is why it's important to look at the RNFL cross section, not just the RNFL classifications.

Visual fields correlate with ONH appearance/ganglion cells and not RNFL scan





Visual fields correlate with ONH appearance/ganglion cells and not RNFL scan



- The patient even had central visual field loss in the right eye.
- If we had looked at the RNFL in a vacuum, assumed all was normal and not tested further, this would have been missed.

Question 4: If your patient has confirmed glaucoma, are they progressing and what is the rate of progression?

- **Normative databases are of limited value in OCT as they generally exclude those with high refractive error, largely consist of European decent patients and do not include any co-morbidities in their data set.**
- **What structure should we follow for progression faster detection of progression? RNFL vs ganglion cell scans?**
- **In several studies, early glaucoma may be best followed for progression with RNFL and later glaucoma may best be followed with ganglion cell scans**

HHS Public Access
Author manuscript
Ophthalmology. Author manuscript; available in PMC 2019 November 28.

Published in final edited form as:
Ophthalmology. 2017 December ; 124(12 Suppl): S57–S65. doi:10.1016/j.ophtha.2017.07.015.

Detecting structural progression in glaucoma with optical coherence tomography

Andrew J. Tatham, FRCOphth, FRCSEd[1], **Felipe A. Medeiros, M.D., Ph.D.**[2]

[1]Princess Alexandra Eye Pavilion and Department of Ophthalmology, University of Edinburgh, UK.

[2]Visual Performance Laboratory, Duke Eye Center, Duke University, USA

Abstract

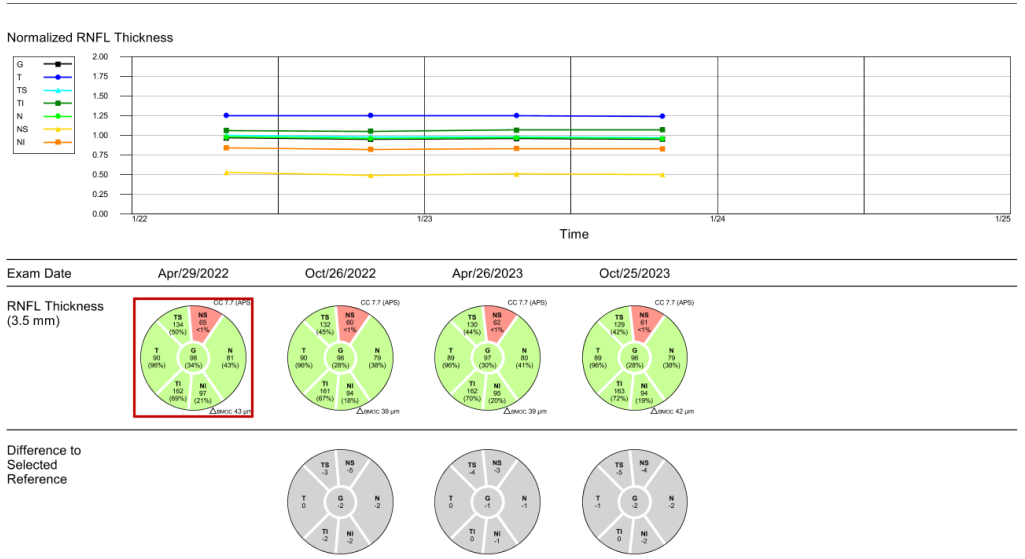
Optical coherence tomography (OCT) is increasingly used to obtain objective measurements of the retinal nerve fiber layer (RNFL), optic nerve head and macula for assessing glaucoma progression. Although OCT has been widely adopted in clinical practice, uncertainty remains concerning how it should be best utilized. Questions include: What is the best structure to measure? What quantity of change is significant? Are structural changes relevant to the patient? How are longitudinal measurements affected by aging, and how can changes due to aging be differentiated from true progression? How should OCT be used alongside visual fields, and how often should OCT be performed? Recent studies have addressed some of these questions.

Important developments include appreciation of the need to use a consistent point of reference for structural measurements, leading to the introduction of Bruch's membrane opening (BMO)–based measures including BMO-minimum rim width and BMO-minimum rim area. Commercially available OCT devices also permit analysis of macular changes over time, for example, changes in the ganglion cell and inner plexiform layers, the sites of the retinal ganglion cell bodies and dendrites, respectively. Several longitudinal studies have compared rates of change in RNFL and macular measurements, with some suggesting the relative value of each parameter may differ at different stages of disease. In early disease, looking for change over time may also be useful for glaucoma diagnosis, with advantages over classifying eyes using cross-sectional normative databases.

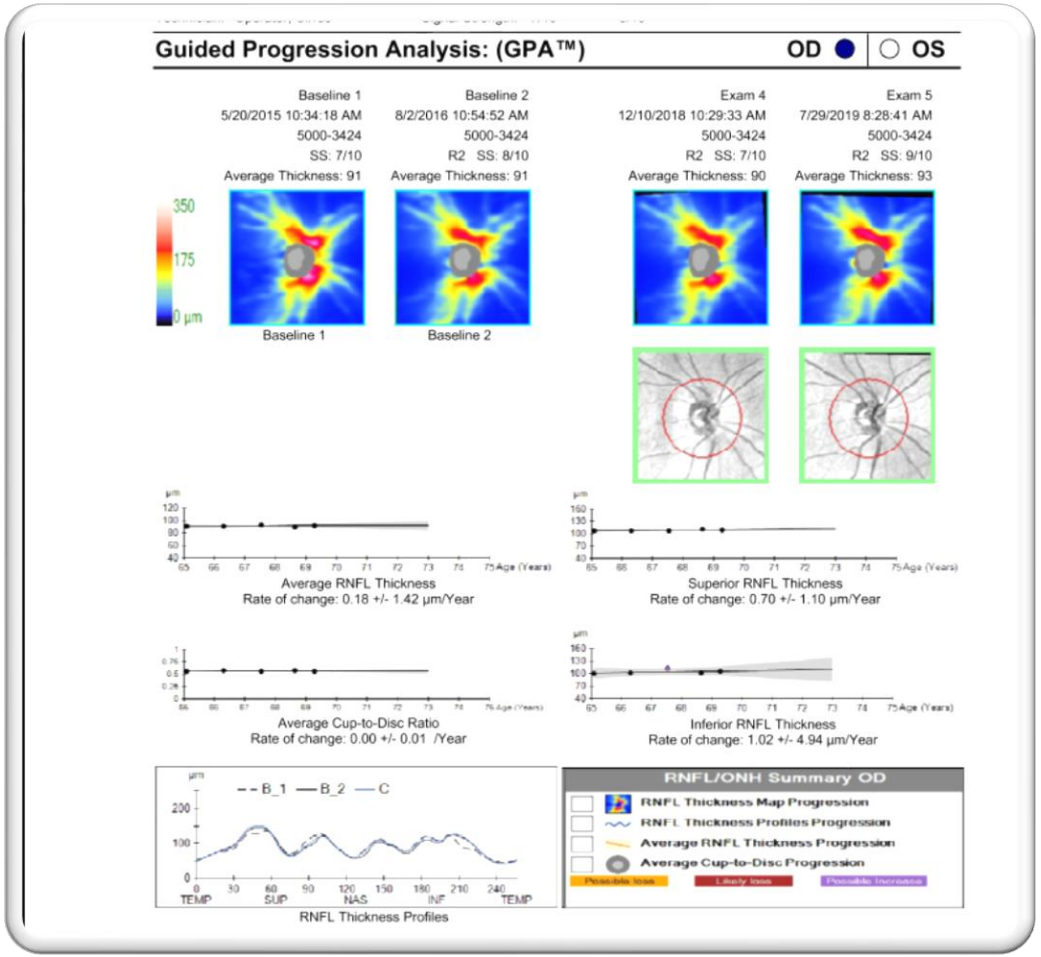
Optimal glaucoma management requires information from imaging and visual fields and efforts have been made to combine information, reducing the noise inherent in both tests to benefit from their different performances according to the stage of the disease. Combining information from different structural measurement may also be useful. There is now substantial evidence that progressive structural changes are of direct clinical relevance, with progressive changes on OCT often preceding functional loss and patients with faster change on OCT at increased risk of worsening visual losses. Identification of such patients offers the possibility of commencing or escalating treatment at an earlier stage. This review appraises recent developments in the use of

Progression and the OCT

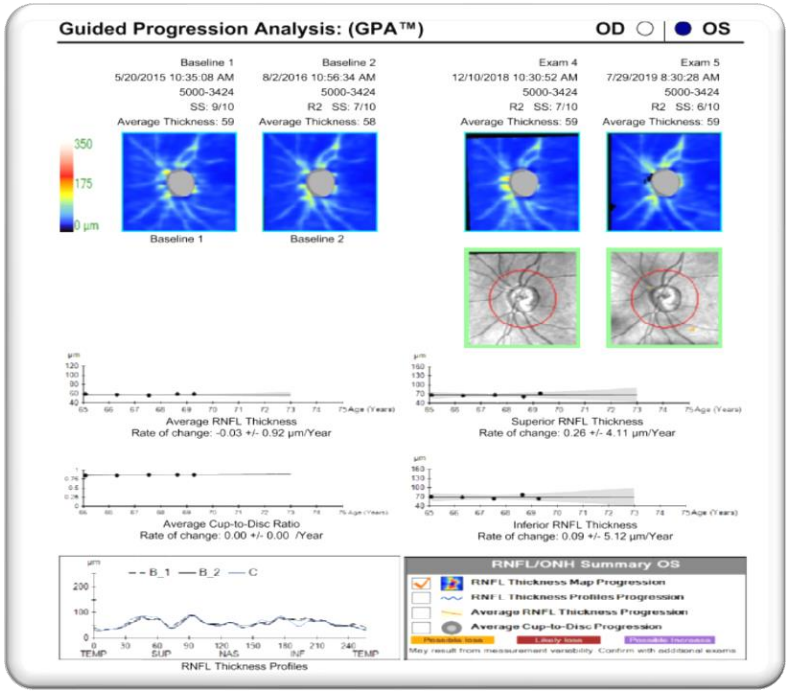
- **Most** useful function of the OCT
  - Monitoring for change over time
- **Event Analysis**
  - Change that is beyond expected variability
  - Today's exam compared to baseline exam
- **Trend Analysis**
  - Rate of change over time
  - Over several visits
  - Linear analysis



Zeiss guided progression analysis

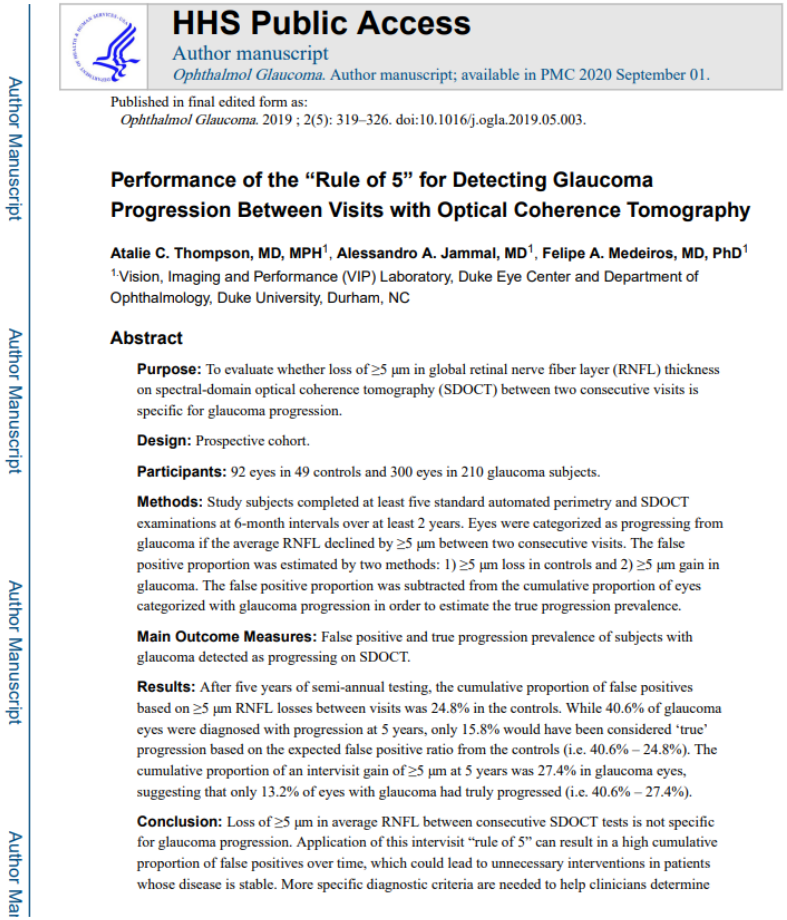


- **First two images are used as a baseline**
- **Subsequent images are referenced to the baseline**



The “Rule of 5?”

- **5 um is commonly used to determine if there is progression on RNFL damage in glaucoma**
- **This study looked at 92 eyes in 49 control patients and 300 eyes in 210 glaucoma patients. These patients were given at LEAST semi-annual VFs and OCT RNFL scans for at LEAST 2 years with a minimum of 5 scans.**
- **After 5 years of study, the false positive rate in progression for the controls was 24.8%. There was progression in 40.6% of the glaucomatous eyes, but this would have been 13.2% when factoring out false positives and RNFL gain.**



Published in final edited form as:
Ophthalmol Glaucoma. 2019 ; 2(5): 319–326. doi:10.1016/j.ogla.2019.05.003.

Performance of the “Rule of 5” for Detecting Glaucoma Progression Between Visits with Optical Coherence Tomography

Atalie C. Thompson, MD, MPH[1], **Alessandro A. Jammal, MD**[1], **Felipe A. Medeiros, MD, PhD**[1]
[1]Vision, Imaging and Performance (VIP) Laboratory, Duke Eye Center and Department of Ophthalmology, Duke University, Durham, NC

Abstract

Purpose: To evaluate whether loss of ≥5 μm in global retinal nerve fiber layer (RNFL) thickness on spectral-domain optical coherence tomography (SDOCT) between two consecutive visits is specific for glaucoma progression.

Design: Prospective cohort.

Participants: 92 eyes in 49 controls and 300 eyes in 210 glaucoma subjects.

Methods: Study subjects completed at least five standard automated perimetry and SDOCT examinations at 6-month intervals over at least 2 years. Eyes were categorized as progressing from glaucoma if the average RNFL declined by ≥5 μm between two consecutive visits. The false positive proportion was estimated by two methods: 1) ≥5 μm loss in controls and 2) ≥5 μm gain in glaucoma. The false positive proportion was subtracted from the cumulative proportion of eyes categorized with glaucoma progression in order to estimate the true progression prevalence.

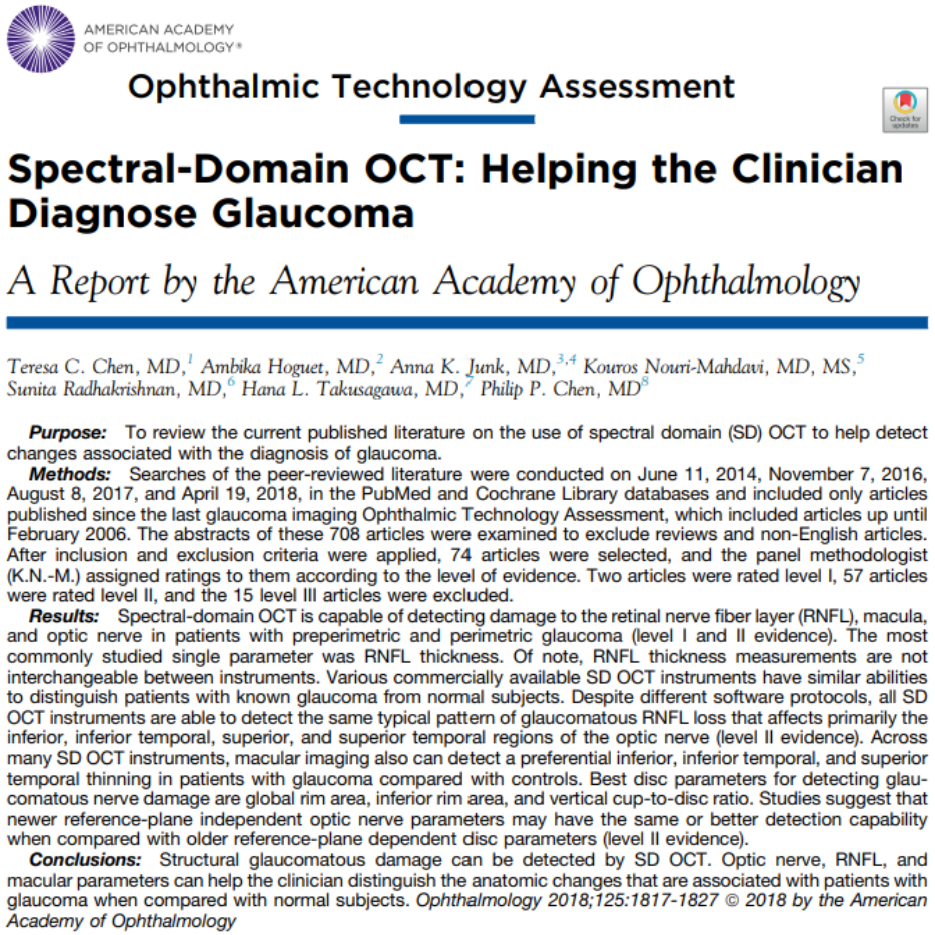
Main Outcome Measures: False positive and true progression prevalence of subjects with glaucoma detected as progressing on SDOCT.

Results: After five years of semi-annual testing, the cumulative proportion of false positives based on ≥5 μm RNFL losses between visits was 24.8% in the controls. While 40.6% of glaucoma eyes were diagnosed with progression at 5 years, only 15.8% would have been considered ‘true’ progression based on the expected false positive ratio from the controls (i.e. 40.6% – 24.8%). The cumulative proportion of an intervisit gain of ≥5 μm at 5 years was 27.4% in glaucoma eyes, suggesting that only 13.2% of eyes with glaucoma had truly progressed (i.e. 40.6% – 27.4%).

Conclusion: Loss of ≥5 μm in average RNFL between consecutive SDOCT tests is not specific for glaucoma progression. Application of this intervisit “rule of 5” can result in a high cumulative proportion of false positives over time, which could lead to unnecessary interventions in patients whose disease is stable. More specific diagnostic criteria are needed to help clinicians determine

Remember the Reliability/resolution of scans

- **Cirrus:**
  - **Reliability: signal strength at least 6**
  - **Axial resolution: 5 um**
- **RTVue:**
  - **Reliability: signal strength at least 30 or 45 (depending on the study)**
  - **Axial resolution: 5 um**
- **Spectralis:**
  - **Reliability: at least 15 (I use 20)**
  - **Axial resolution: 7 um**



AMERICAN ACADEMY OF OPHTHALMOLOGY®

Ophthalmic Technology Assessment

Spectral-Domain OCT: Helping the Clinician Diagnose Glaucoma

A Report by the American Academy of Ophthalmology

Teresa C. Chen, MD,[1] Ambika Hoguet, MD,[2] Anna K. Junk, MD,[3,4] Kouros Nouri-Mahdavi, MD, MS,[5] Sunita Radhakrishnan, MD,[6] Hana L. Takusagawa, MD,[7] Philip P. Chen, MD[8]

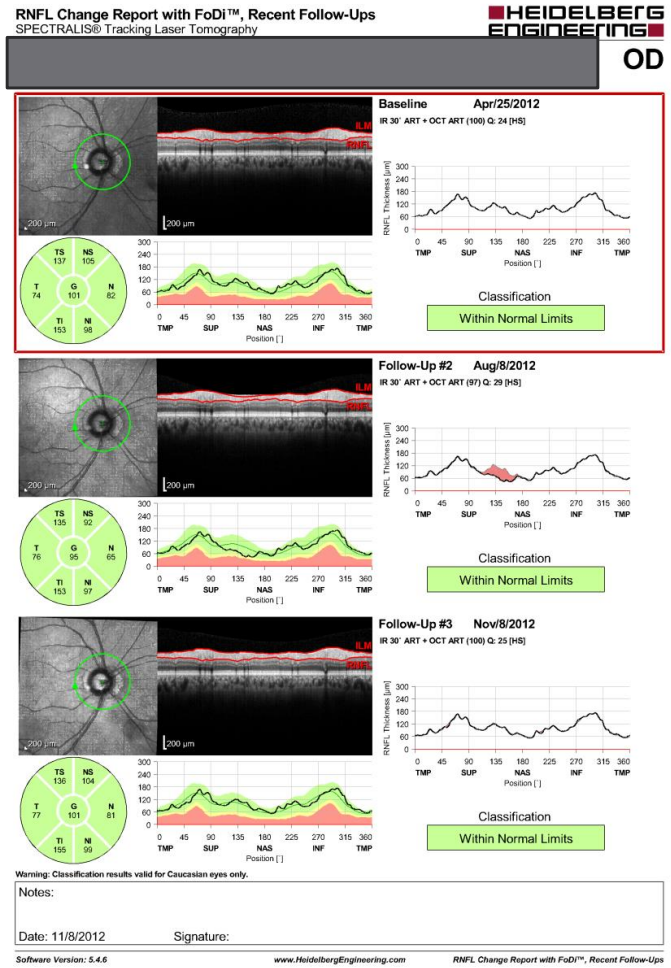
Purpose: To review the current published literature on the use of spectral domain (SD) OCT to help detect changes associated with the diagnosis of glaucoma.

Methods: Searches of the peer-reviewed literature were conducted on June 11, 2014, November 7, 2016, August 8, 2017, and April 19, 2018, in the PubMed and Cochrane Library databases and included only articles published since the last glaucoma imaging Ophthalmic Technology Assessment, which included articles up until February 2006. The abstracts of these 708 articles were examined to exclude reviews and non-English articles. After inclusion and exclusion criteria were applied, 74 articles were selected, and the panel methodologist (K.N.-M.) assigned ratings to them according to the level of evidence. Two articles were rated level I, 57 articles were rated level II, and the 15 level III articles were excluded.

Results: Spectral-domain OCT is capable of detecting damage to the retinal nerve fiber layer (RNFL), macula, and optic nerve in patients with preperimetric and perimetric glaucoma (level I and II evidence). The most commonly studied single parameter was RNFL thickness. Of note, RNFL thickness measurements are not interchangeable between instruments. Various commercially available SD OCT instruments have similar abilities to distinguish patients with known glaucoma from normal subjects. Despite different software protocols, all SD OCT instruments are able to detect the same typical pattern of glaucomatous RNFL loss that affects primarily the inferior, inferior temporal, superior, and superior temporal regions of the optic nerve (level II evidence). Across many SD OCT instruments, macular imaging also can detect a preferential inferior, inferior temporal, and superior temporal thinning in patients with glaucoma compared with controls. Best disc parameters for detecting glaucomatous nerve damage are global rim area, inferior rim area, and vertical cup-to-disc ratio. Studies suggest that newer reference-plane independent optic nerve parameters may have the same or better detection capability when compared with older reference-plane dependent disc parameters (level II evidence).

Conclusions: Structural glaucomatous damage can be detected by SD OCT. Optic nerve, RNFL, and macular parameters can help the clinician distinguish the anatomic changes that are associated with patients with glaucoma when compared with normal subjects. *Ophthalmology 2018;125:1817-1827 © 2018 by the American Academy of Ophthalmology*

Progression not confirmed



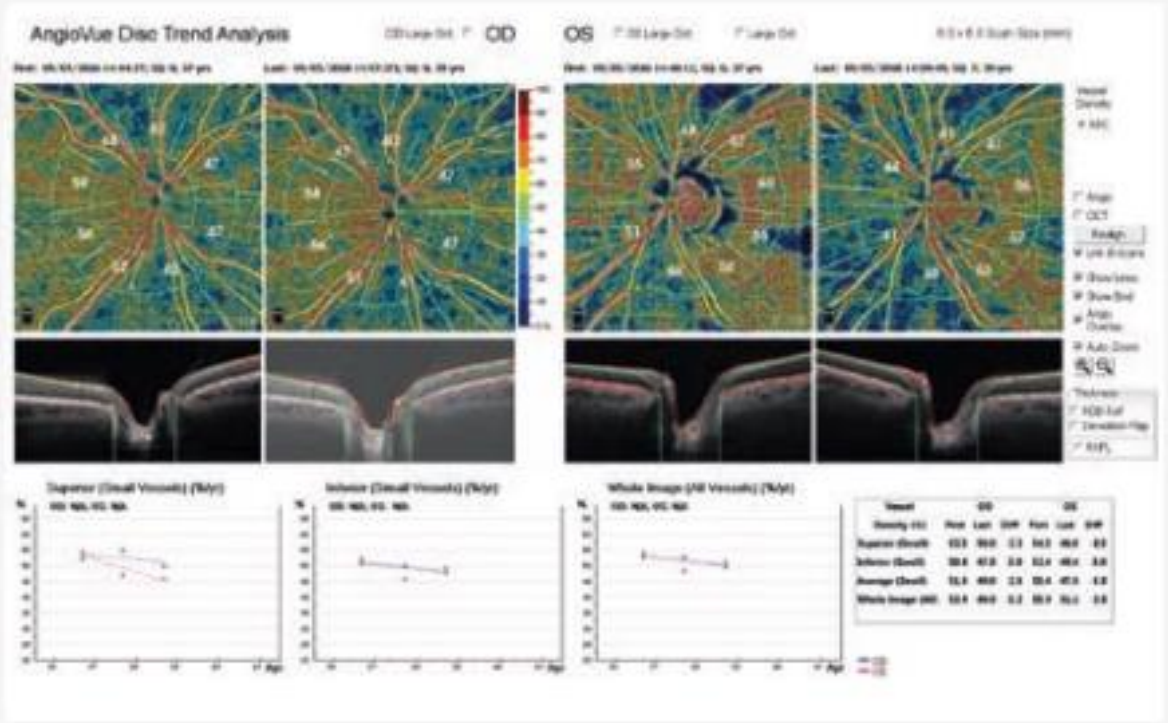
- **Try not to change therapy/start management based on one single progression on the OCT.**

- **Instead, repeat the scan and see if progression is confirmed.**

Progression via OCT A

AngioDisc Trend Analysis Report

Measure the vessel density of the RPCs, assess visit-to-visit change, and estimate rate of change in glaucoma patients and suspects. Vessel density analysis complements RNFL and GCC analysis and aids in the management of advanced glaucoma – especially in cases where neural structural measurements have reached the measurement floor.



https://www.visionix.com/wp-content/uploads/2022/10/BrochureEN-OPTOVUE-SOLIX-ESSENTIAL-ind10-0322-WEB-3.pdf

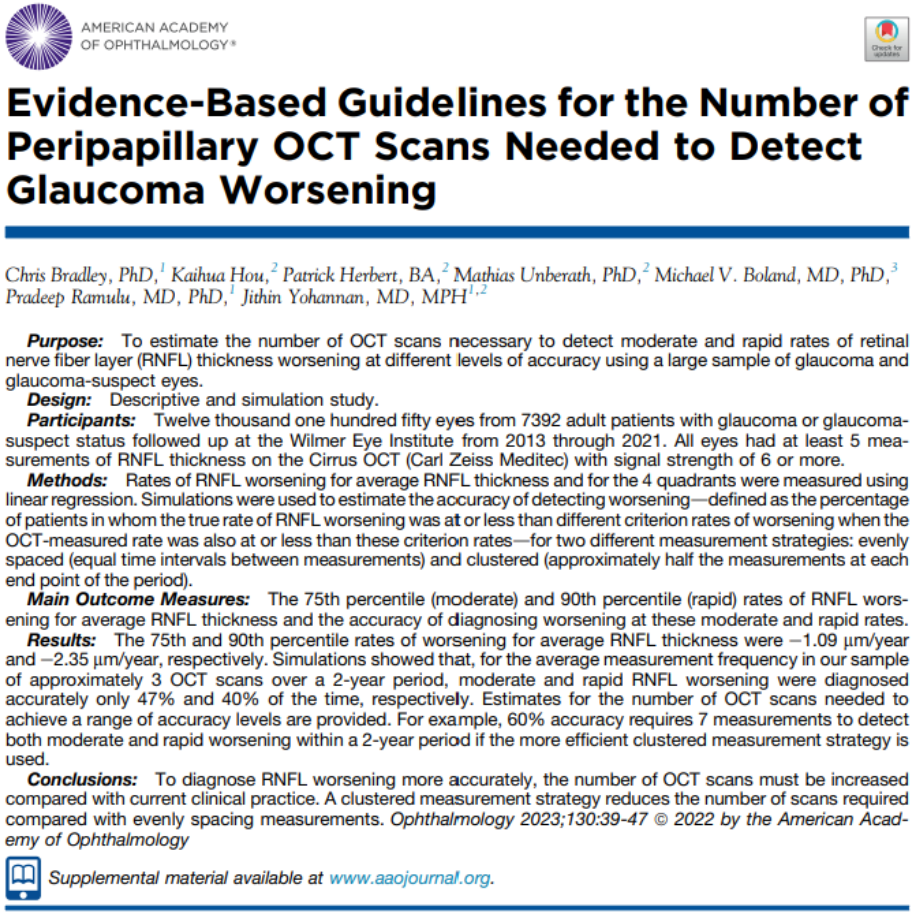
Frequency of scans?

- **African Descent and Glaucoma Evaluation Study (ADAGES) tried to look at the differences in glaucoma onset between individuals of African and European descent.**
- **2 tests were given at baseline and then at 4,6,12 or 24 month intervals.**
- **Progression was confirmed with a significant RNFL loss at two consective visits (-1um/year – average progressor, -2.5 um/year – rapid progressor)**
- **6 month testing interval provided the best trade-off for following glaucoma patients with OCT RNFL, although some higher risk patients should be tested at 4 month intervals.**

Melchior, Bruna MD*,†; De Moraes, Carlos G. MD, PhD, MPH*; Paula, Jayter S. MD, PhD†; Cioffi, George A. MD*; Girkin, Christopher A. MD, MSPH‡; Fazio, Massimo A. PhD‡; Weinreb, Robert N. MD§; Zangwill, Linda M. PhD§; Liebmann, Jeffrey M. MD*. Frequency of Optical Coherence Tomography Testing to Detect Progression in Glaucoma. Journal of Glaucoma 31(11):p 854-859, November 2022. | DOI: 10.1097/IJG.0000000000002101

Number of scans to determine progression on OCT?

- Found that to detect OCT RNFL worsening using 3 RNFL scans over 2 years, you would only detect 47% of the time for moderate progression and 40% of the time for rapid progressors.



AMERICAN ACADEMY OF OPHTHALMOLOGY®

Evidence-Based Guidelines for the Number of Peripapillary OCT Scans Needed to Detect Glaucoma Worsening

Chris Bradley, PhD,[1] Kaihua Hou,[2] Patrick Herbert, BA,[2] Mathias Unberath, PhD,[2] Michael V. Boland, MD, PhD,[3] Pradeep Ramulu, MD, PhD,[1] Jithin Yohannan, MD, MPH[1,2]

Purpose: To estimate the number of OCT scans necessary to detect moderate and rapid rates of retinal nerve fiber layer (RNFL) thickness worsening at different levels of accuracy using a large sample of glaucoma and glaucoma-suspect eyes.

Design: Descriptive and simulation study.

Participants: Twelve thousand one hundred fifty eyes from 7392 adult patients with glaucoma or glaucoma-suspect status followed up at the Wilmer Eye Institute from 2013 through 2021. All eyes had at least 5 measurements of RNFL thickness on the Cirrus OCT (Carl Zeiss Meditec) with signal strength of 6 or more.

Methods: Rates of RNFL worsening for average RNFL thickness and for the 4 quadrants were measured using linear regression. Simulations were used to estimate the accuracy of detecting worsening—defined as the percentage of patients in whom the true rate of RNFL worsening was at or less than different criterion rates of worsening when the OCT-measured rate was also at or less than these criterion rates—for two different measurement strategies: evenly spaced (equal time intervals between measurements) and clustered (approximately half the measurements at each end point of the period).

Main Outcome Measures: The 75th percentile (moderate) and 90th percentile (rapid) rates of RNFL worsening for average RNFL thickness and the accuracy of diagnosing worsening at these moderate and rapid rates.

Results: The 75th and 90th percentile rates of worsening for average RNFL thickness were −1.09 μm/year and −2.35 μm/year, respectively. Simulations showed that, for the average measurement frequency in our sample of approximately 3 OCT scans over a 2-year period, moderate and rapid RNFL worsening were diagnosed accurately only 47% and 40% of the time, respectively. Estimates for the number of OCT scans needed to achieve a range of accuracy levels are provided. For example, 60% accuracy requires 7 measurements to detect both moderate and rapid worsening within a 2-year period if the more efficient clustered measurement strategy is used.

Conclusions: To diagnose RNFL worsening more accurately, the number of OCT scans must be increased compared with current clinical practice. A clustered measurement strategy reduces the number of scans required compared with evenly spacing measurements. *Ophthalmology 2023;130:39-47 © 2022 by the American Academy of Ophthalmology*

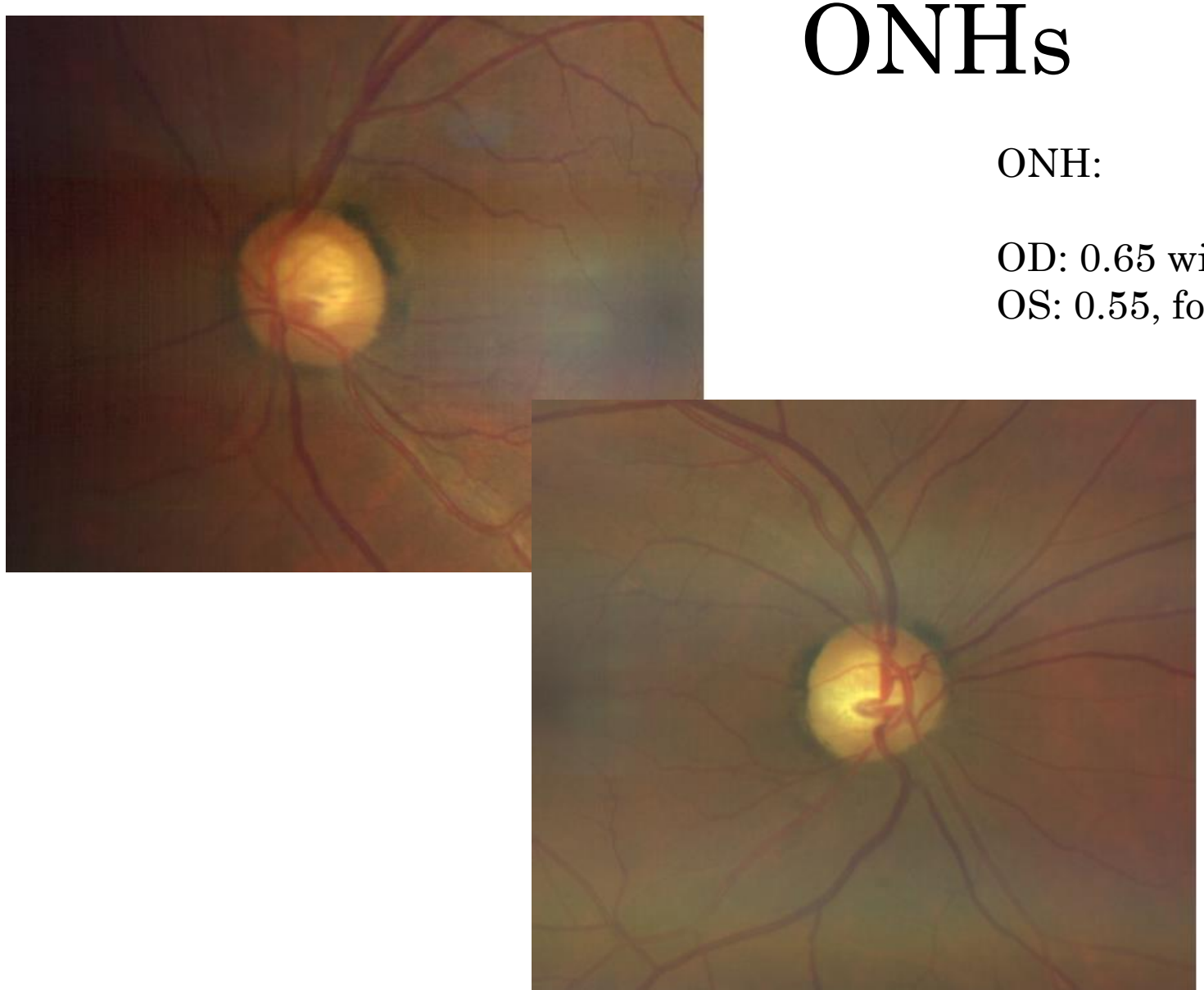
Supplemental material available at www.aaojournal.org.

Remember to reset the baseline!

Case 1

- **61 year old AA male.**
- **Presents for first examination at the VA**
- **No complaints.**
- **Past medical history: HTN. DM**
- **Past ocular history: exam 2 years prior. Mild cataracts OU**
- **Correctable to 20/20 OD/OS**
- **IOP 17/17**
- **Dilated and…….**

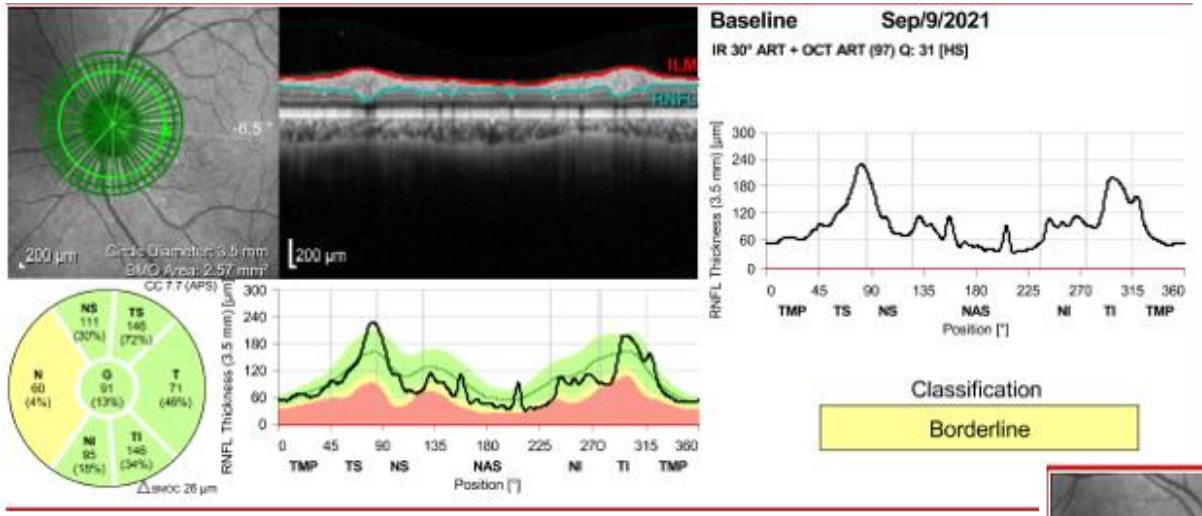
ONHs

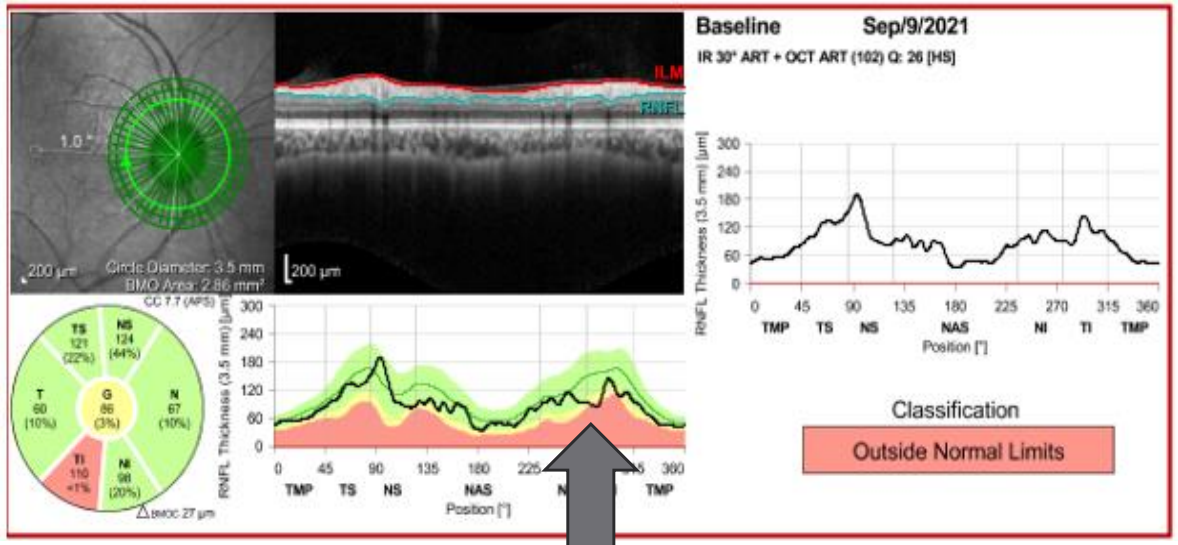


ONH:

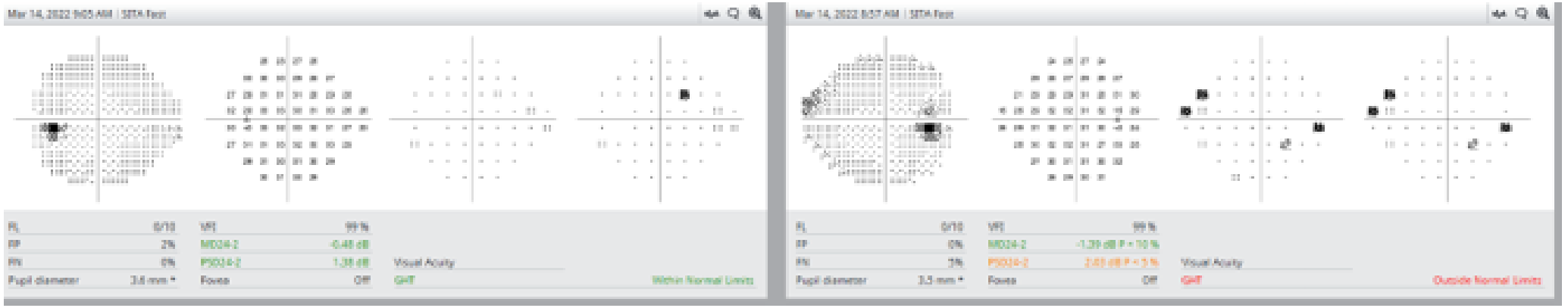
OD: 0.65 with a thin inferior rim
OS: 0.55, follows ISNT rule

OCT RNFL


Baseline
Sep/9/2021
IR 30° ART + OCT ART (97) Q: 31 [HS]
ILM
RNFL
200 µm
Circle Diameter: 3.5 mm
BMO Area: 2.57 mm²
CC 7.7 (APS)
RNFL Thickness (3.5 mm) [µm]
Position [°]
TMP TS NS NAS NI TI TMP
Classification
Borderline


Baseline
Sep/9/2021
IR 30° ART + OCT ART (102) Q: 26 [HS]
ILM
RNFL
200 µm
Circle Diameter: 3.5 mm
BMO Area: 2.86 mm²
CC 7.7 (APS)
RNFL Thickness (3.5 mm) [µm]
Position [°]
TMP TS NS NAS NI TI TMP
Classification
Outside Normal Limits

Visual fields

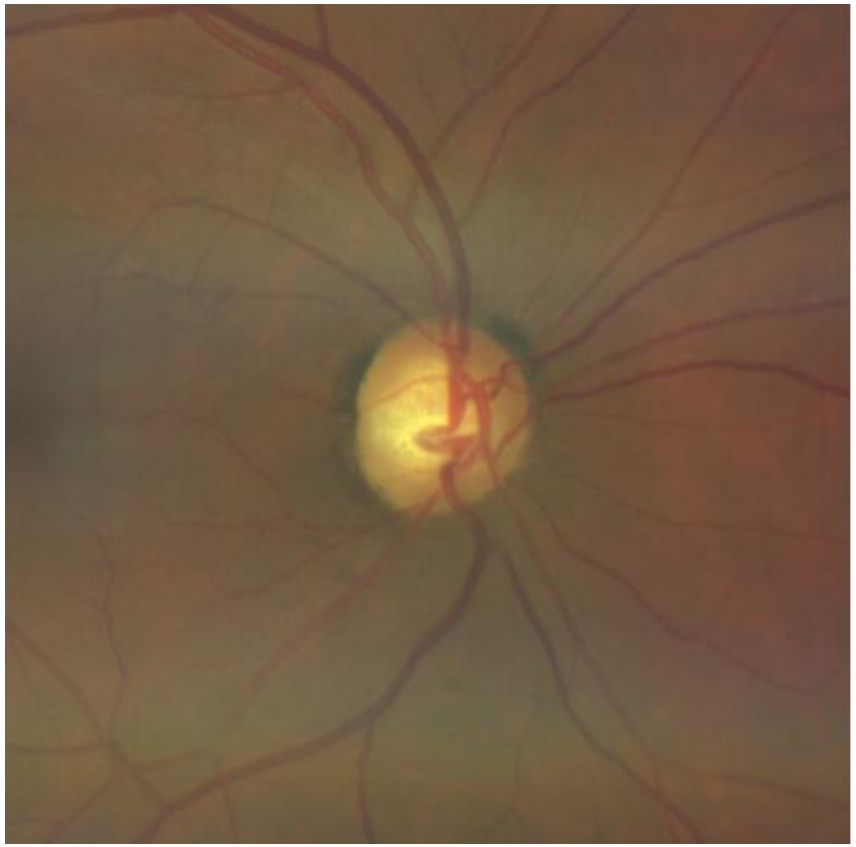


24-2 SITA Fast

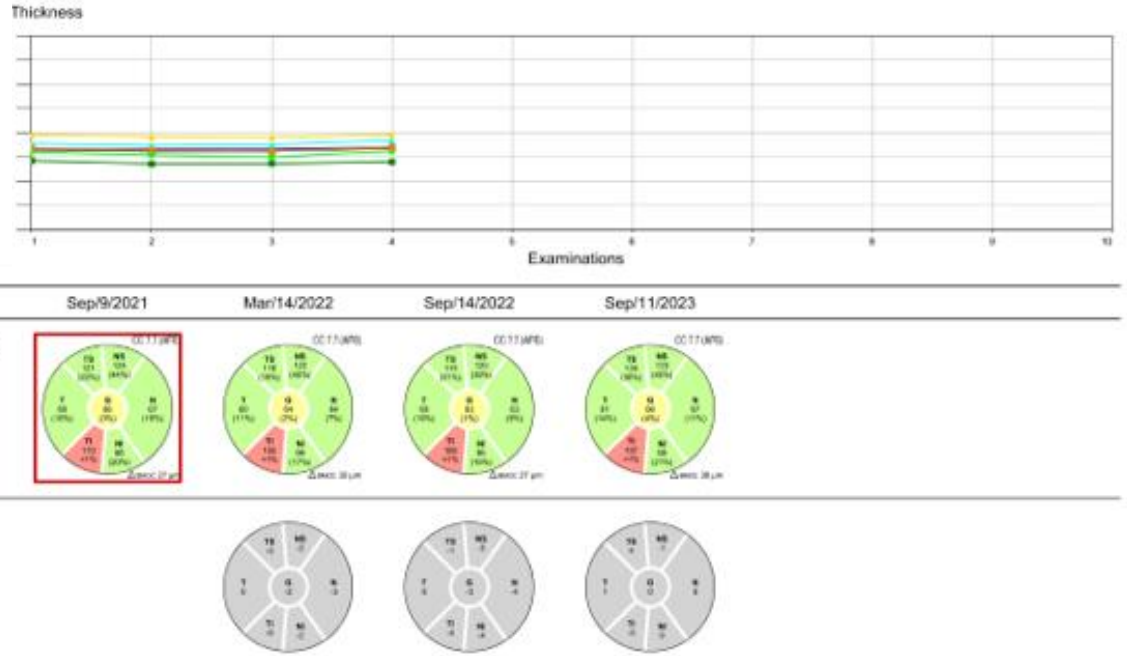
OD: reliable, GHT: ONL. Superior nasal step consistent with ONH, OCT RNFL appearance
OS: reliable, GHT: WNL, no significant cluster defects

Diagnosis

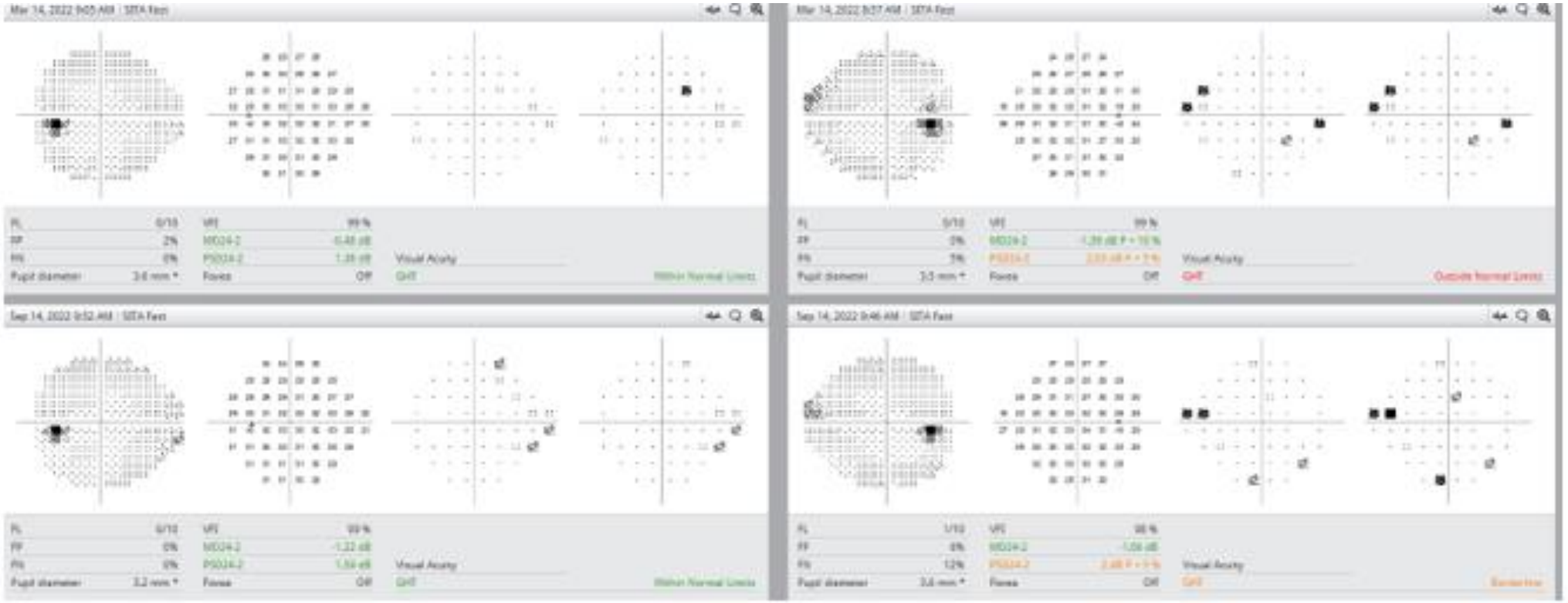
- **Pt was diagnosed with NTG OD, NTG suspect OS**
- **More information:**
  - **Tmax: 17/17**
  - **Pach: 573/568**
  - **Angles open to CBB 360 per gonioscopy**
  - **Pt was started on Latanoprost QHS OU**



OCT stable without progression.



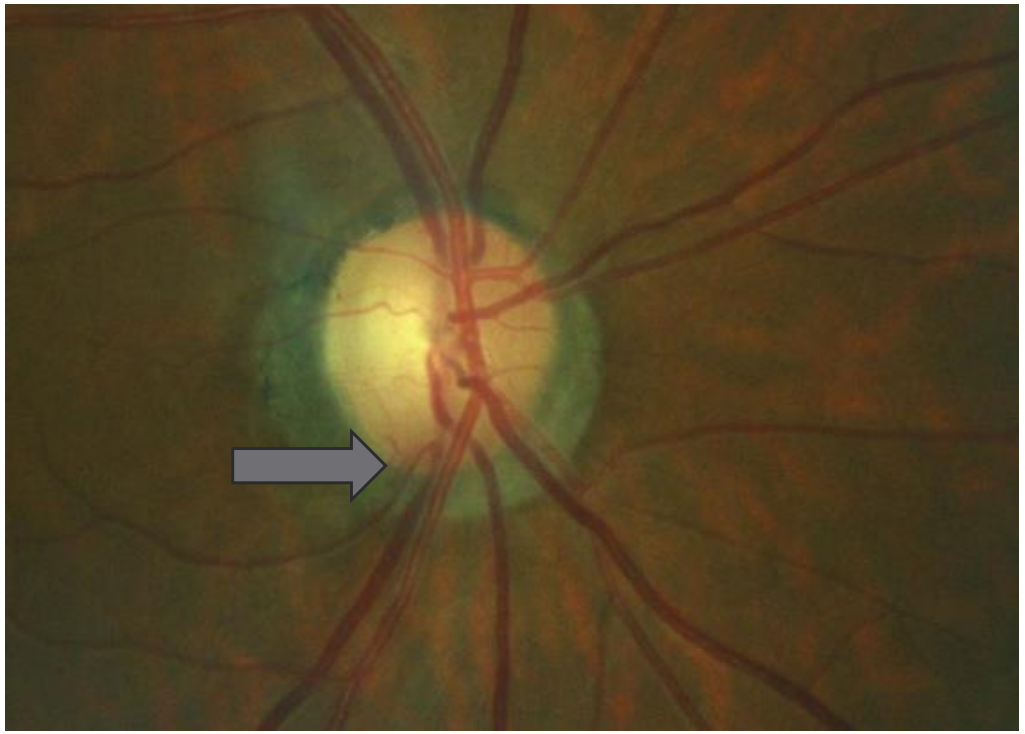
VFs stable without progression



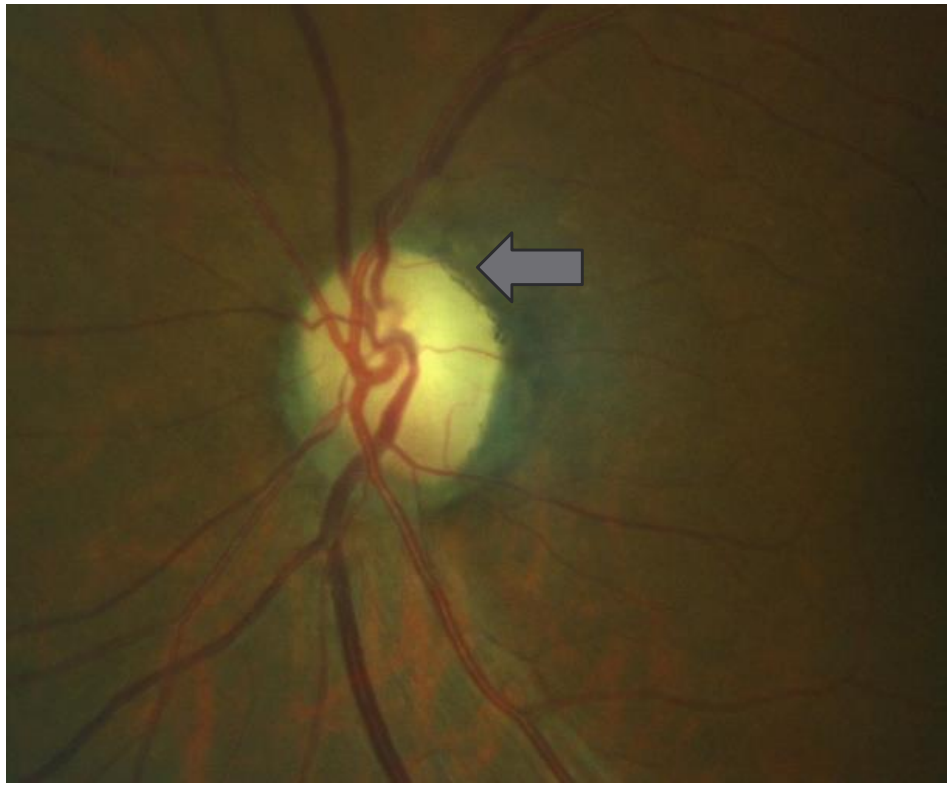
Case 2

- 73 yo AA male.
- Pt comes in after being lost to f/u x 2 years….
- Ocular history:
  - 1. Open angle glaucoma suspect OU based on ONH appearance/IOP
    - OD: 0.50, tilted temporally, height = 1.7 mm c 78 D lens
    - OS: 0.50, pallor superiorly
    - PACH: 503/514
    - Tmax: 25/21
    - Angles open per gonioscopy
  - 2. Past NAION OS
- Acuities:
  - OD: 20/25+
  - OS: 20/30-2
- Pupils: ERRL (+) Left APD
- Anterior segment unremarkable
- Goldmann IOP:
  - OD: 26 mmHG
  - OS: 18 mmHG @ 8:30 am

ONHs

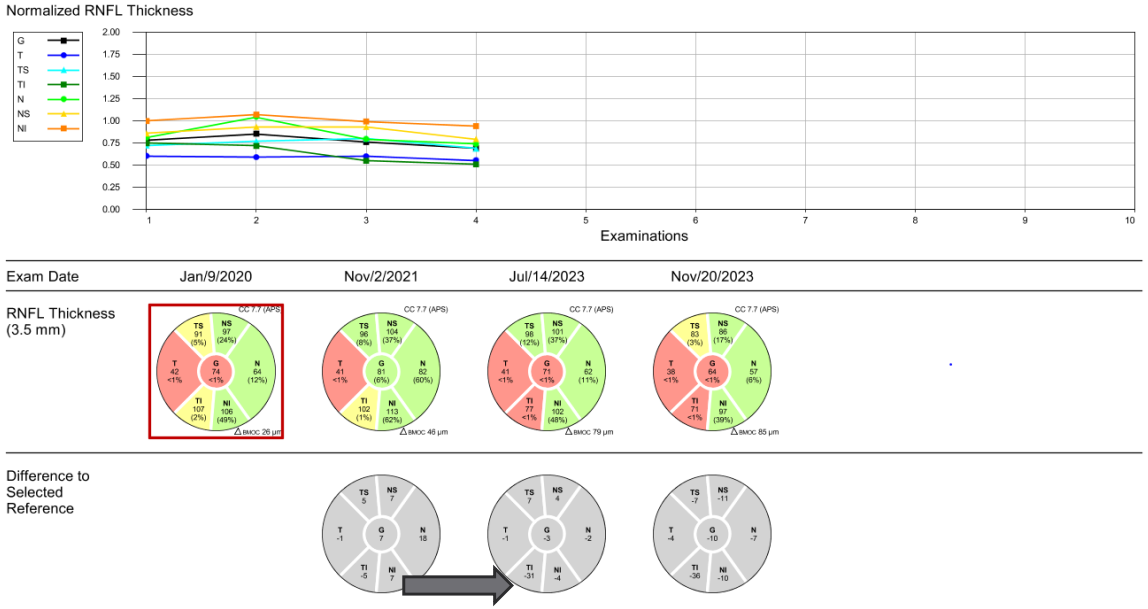


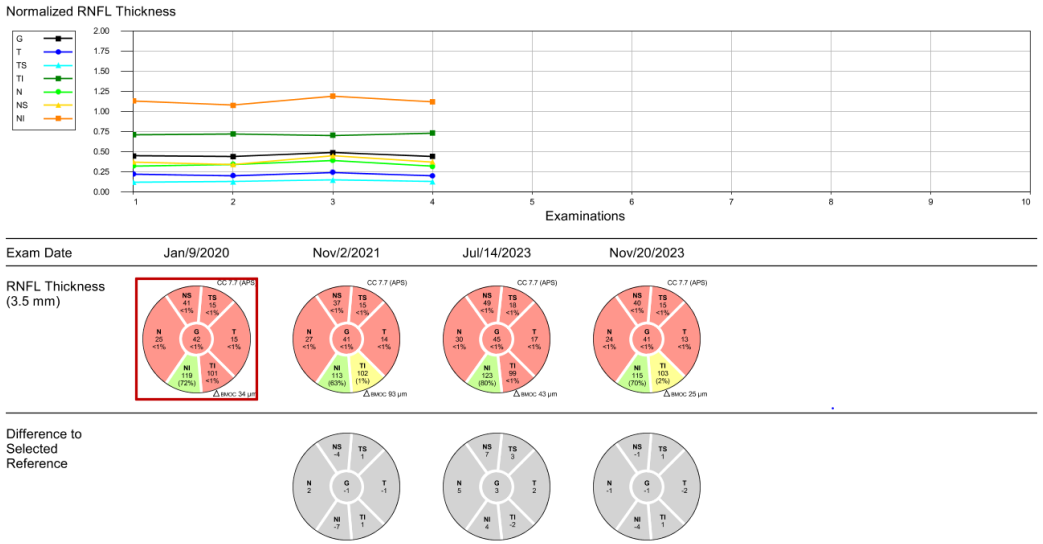
Now with noted thinning of the inferior rim



Still with superior temporal pallor

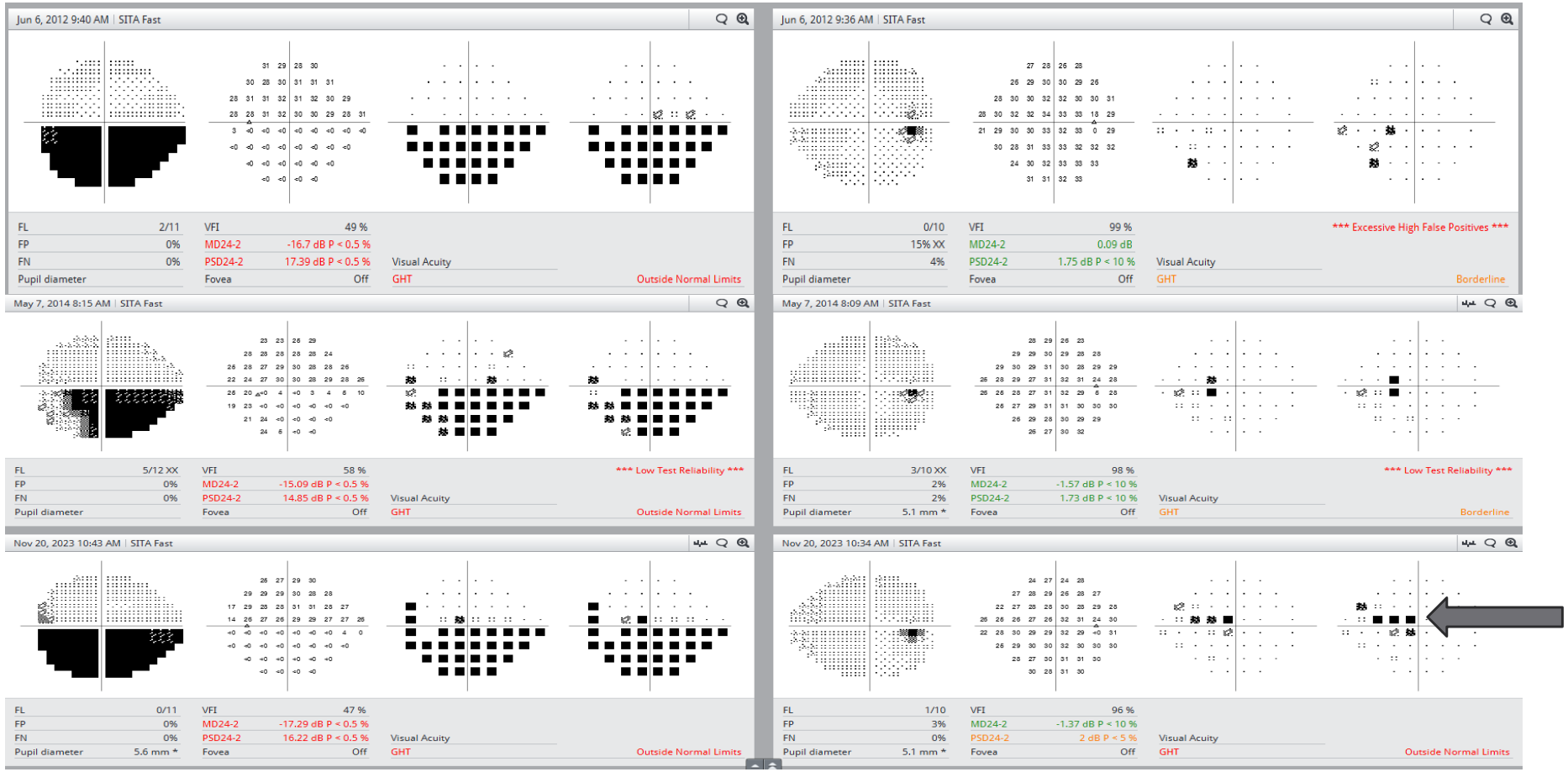
OCT RNFL





Significant progression inferior temporally. Pt was asked to return to confirm progression on OCT and to get an updated VF exam. OCT RNFL progression was <u>confirmed</u> on subsequent exam

Visual fields



Now with a superior nasal defect consistent with OCT RNFL changes and into central field.

Diagnosis

- Pt was diagnosed with moderate glaucoma OD and started on latanoprost.
- He was scheduled to come back for a 10-2 SF OD to see the extent of the visual field loss from glaucoma.