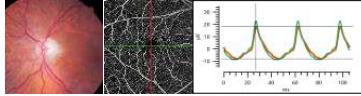


Utilizing the latest diagnostic technology in the management of ocular disease

Michael Cymbor, OD, FAAO
COPE 72419-PD



Disclosure

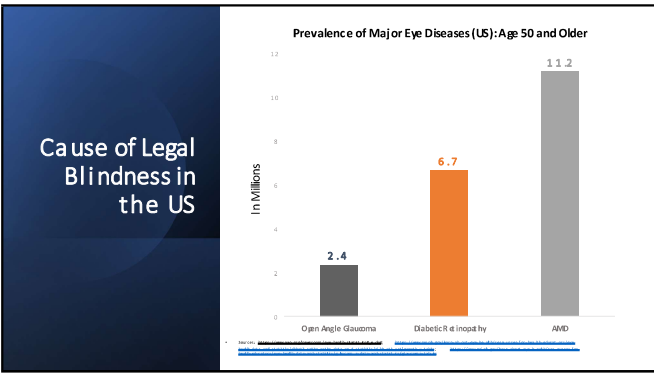
- Key opinion leader and speaker for:
 - Optovue
 - Quidel
 - New World Medical
 - LKC Technologies

NITTANY EYE ASSOCIATES



Ways to get in touch

- www.mikecymbor.com
 - Handouts
 - Webinars
- mcymbor@nittaneye.com
- LinkedIn



NIH News Release

Visual impairment, blindness cases in U.S. expected to double by 2050

NIH-funded studies tease out trends by race, ethnicity and sex.

With the youngest of the baby boomers hitting 65 by 2028, the number of people with visual impairment or blindness in the United States is expected to double to more than 8 million by 2050, according to projections based on the most recent census data and from studies funded by the National Eye Institute, part of the National Institutes of Health. Another 16.4 million Americans are expected to have difficulty seeing due to correctable refractive errors such as myopia (nearsightedness) or hyperopia (farsightedness) that can be fixed with glasses, contacts or surgery.

The researchers were led by Rohit Varma, M.D., director of the University of

Increased Demand for Medical Eye Care

20 million more routine and medical eye exams will be required in 2025 than were needed in 2015, and this number will continue to increase every year for the foreseeable future

The number of FTE optometrists will increase by 13% between 2015 and 2025

The number of FTE ophthalmologists will increase by 2.1% between 2015 and 2025

"The future of Optometry in America", Richard Edlow, OD. Modern Optometry March 2019

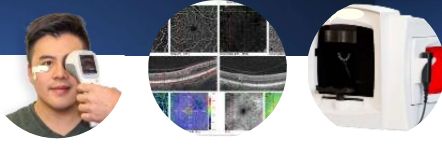
Imbalance of supply/demand



Our patient trying to get an appointment



Three Technologies



ERG

OCT-A

Dark Adaptation

Click to add text

- Measures the electrical responses of various cell types in the retina, including:
 - photoreceptors
 - rods and cones
 - inner retinal cells
 - bipolar and amacrine cells
 - ganglion cells

in response to a stimulus

Electroretinography

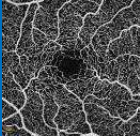
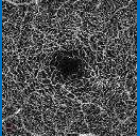

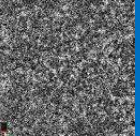
The ERG Waveform

A Wave
Photoreceptor Function, primarily driven by cones

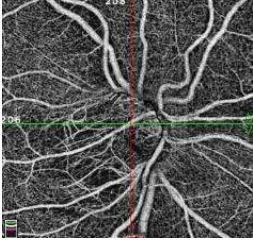

B Wave
Bipolar Cell Function, inserts signal from photoreceptors and transmits to the inner retina.

PhNR
Function of the innermost retinal layer, Retinal Ganglion Cell.

OCT Angiography (OCT-A)

			
Superficial Capillary Plexus	Deep Capillary Plexus	Outer Retinal Zone	Choriocapillaris
Larger Vessels Smaller FAZ than Deep Plexus	Network of Fine Capillaries Larger FAZ	Avascular	Homogeneous Flow

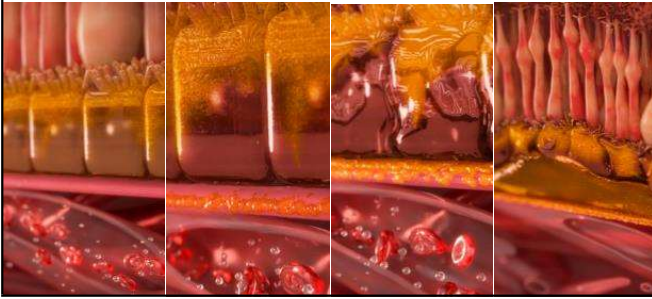
OCT-A

	
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Dark Adaptation

AMD Disease Process

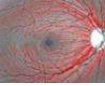





Three Ocular Disease States

	Glaucoma	Diabetic Retinopathy	AMD
Structure	Photos/OCT	Photos/OCT	Photos/OCT
Function	Visual Fields	?	?
Early Diagnosis	ERG/OCT-A	ERG/OCT-A	Dark Adaptation/OCT-A (w/et)

	Glaucoma
Structure	Photos/OCT
Function	Visual Fields
Early Diagnosis	ERG/OCT-A

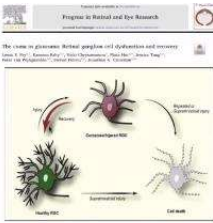
Retinal Ganglion Cells



• There is a growing body of evidence suggesting that, prior to irreversible cell death, compromised retinal ganglion cells (RGCs) enter a dysfunctional state that may partially recover under certain conditions

Retinal ganglion cells can recover



The Coma in Glaucoma

Fry LE, Fahy E, Chrysostomou V, Hui F, Tang J, van Wijngaarden P, Petrou S, Crowston JG. The coma in glaucoma: retinal ganglion cell dysfunction and recovery. *Progress in retinal and eye research*. 2018 Jul 1; 65: 77-92

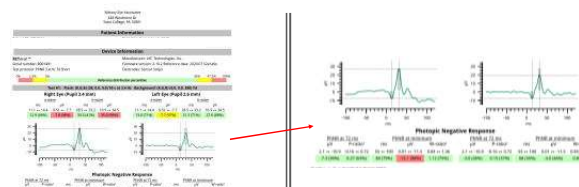
This is where ERG comes in

- The full-field PhNR amplitude provides a potentially reversible measure of inner retinal function that improves after IOP lowering
- Niyadurupola N, Luu CD, Nguyen DQ, Geddes K, Tan GX, Wong CC, Tran T, Coote MA, Crowston JG. Intraocular pressure lowering is associated with an increase in the photopic negative response (PhNR) amplitude in glaucoma and ocular hypertensive eyes. *Investigative ophthalmology & visual science*. 2013 Mar 1; 54(3):1913-9.

Good Correlation between FF ERG, VF, and OCT

- "RETeval (ERG)...correlated well with VF MD and the established global OCT thickness parameters, both in the total glaucoma severity spectrum and in moderate-to-advanced glaucoma"
- Kita Y, Holló G, Saito T, Momota Y, Kita R, Tsunoda K, Hirakata A. RETeval Portable Electroretinogram Parameters in Different Severity Stages of Glaucoma. *Journal of glaucoma*. 2020 Jul 8;29(7):572-80.

PhNR in Glaucoma



"Almost all published articles demonstrated a significant reduction of blood flow, capillary diameter and vascular density in glaucomatous eyes. Interestingly, these differences were detectable even in glaucoma suspects and eyes with preperimetric glaucoma and increased proportional to the severity of glaucoma damage."

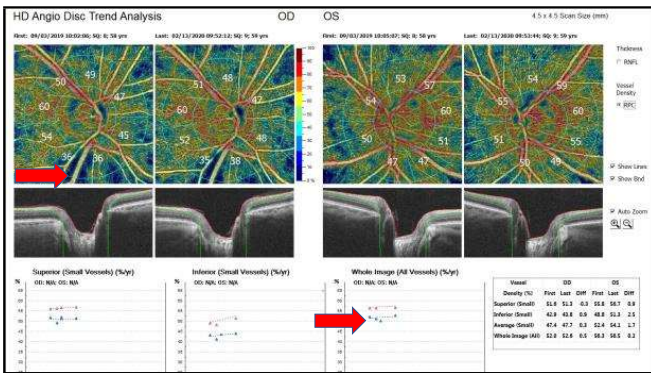
Author	Year of Publication	Study findings
Sab SMI, et al ¹⁰	2004	Peripapillary retinal vascular diameter was lower in 50% of PNVG eyes. This finding was apparent for inner and outer ganglionic lamellae in inferior retina, indicating regional retinal damage in RNFL, inner choroid and inner lamina propria.
Sab SMI, et al ¹⁰	2004	Peripapillary retinal vascular diameter was significantly lower than in glaucoma eyes without such a defect. This difference was significant after adjusting for disease severity.
Ni FK, et al ¹¹	2004	Macular capillary density and the ganglion cell (GC) cell coefficient in the normal eye. GC coefficient density correlated with temporal RNFL thickness and severity of visual field damage.
Kamdemouali A, et al ¹²	2004	In a cohort of 73 healthy subjects, 48 glaucoma suspects and 74 glaucoma patients, volumetric methods in peripapillary RNFL were found to be more sensitive compared to standard thickness and glaucoma-free. The most striking finding was that the association with IOP and MD was stronger than that of RNFL or retinal MD.
Kamdemouali A, et al ¹²	2004	Peripapillary and whole image vascular density measured by OCTA had similar diagnostic accuracy to peripapillary RNFL thickness measurement for detecting glaucoma even in a group of 241 eyes.
Chhabra R, et al ¹³	2007	Peripapillary retinal vascular diameter was significantly lower in glaucoma suspects than in normal eyes. Peripapillary RNFL thickness performed better for identifying PNVG with normal vision.
Lau BJ, et al ¹⁴	2007	Peripapillary capillary density was significantly lower in affected eyes of 14 normal-tension glaucoma compared to unaffected eyes of the same patients and 11 eyes of healthy subjects. Retinal capillary network was independent in the eyes corresponding to RNFL defects. In these cases, choroidal and ONH vessels did not show apparent changes.
Shiós L, et al ¹⁵	2007	FAZ accurately demonstrated a significant association with structural central visual field loss in 74 ONH patients with normal or peripheral visual field damage and FAZ area was correlated with the severity of central visual loss. There was a significant correlation between the retinal capillary density coverage (FAZ) and the thickness of the RNFL.

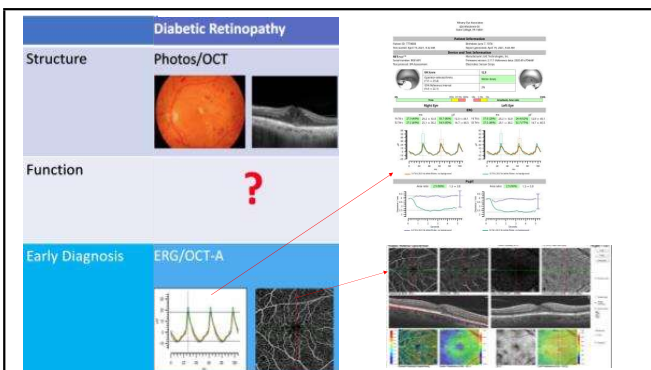
1. Daneshvar R, Nouri-Mahdavi K. Optical Coherence Tomography Angiography: A New Tool in Glaucoma Diagnostics and Research. *J Ophthalmic Vis Res*. 2017;12(3):325-332. doi:10.4103/jovr.jovr_36_17

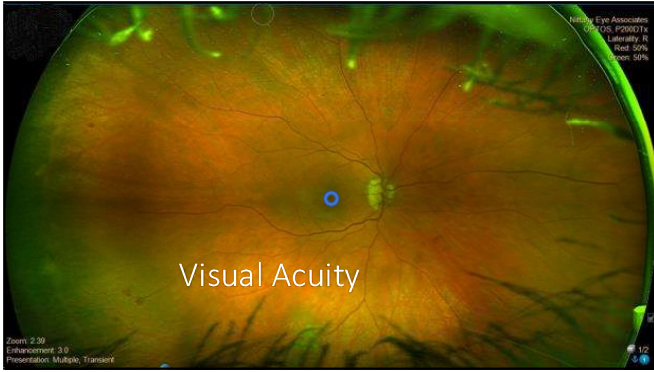
OCT-A in Glaucoma

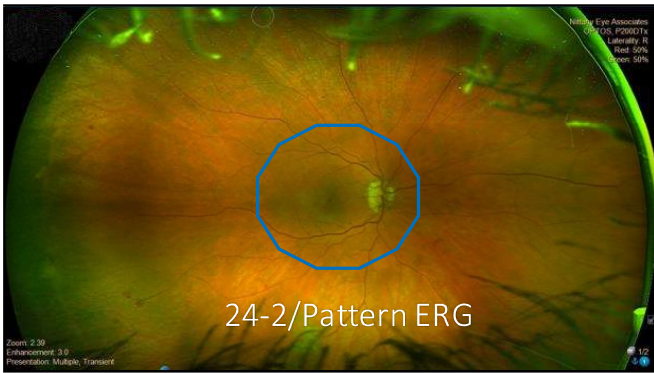
- "OCTA enhanced both the sensitivity and specificity for glaucoma diagnosis."
- "OCTA could accurately detect glaucomatous eyes, which may be misdiagnosed by OCT as normal, and OCTA could detect normal eyes, which may be misdiagnosed by OCT as glaucomatous."
- "Therefore, these two modalities complemented each other in the diagnosis of glaucoma."

Kwon HJ, Kwon J, Sung KR. Additive Role of Optical Coherence Tomography Angiography Vessel Density Measurements in Glaucoma Diagnosis. *Korean J Ophthalmol*. 2019;33(4):315-325












Does diabetic retinal damage precede diabetic retinopathy?

"Our data provide structural and functional evidence to support the hypothesis of neuronal damage in DM, prior to clinically evident vascular changes"

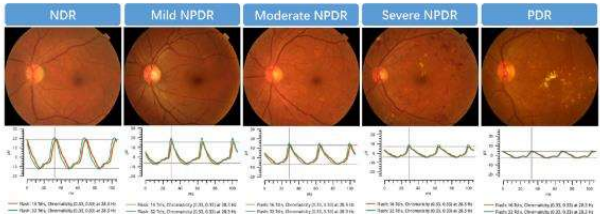
"Our data also confirm that a simple measurement of BCVA might be insufficient to fully characterize the changes in visual function"

None of these findings were correlated with HbA1c or duration of diabetes



- Raza Shah, MD, retinal specialist
- Retinal damage occurs earlier than we currently realize or seem to admit
- We will need to either change definitions or treatment criteria

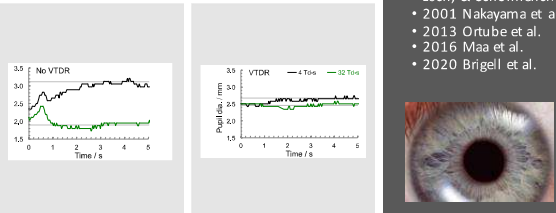
Montesano G, Ornetto G, Higgins BE, Das R, Graham W, Chakravarthy U, McGehee D, Young S, Kim F, Vajith DM, Cizick DP. Evidence for Structural and Functional Damage of the Inner Retina in Diabetes. *Invest Ophthalmol Vis Sci*. 2021 Mar 1;60(3):35.



ERG is an effective screening device at all levels of DR

- Zeng Y, Cao D, Yang D, Zhuang X, Yu H, Hu Y, Zhang Y, Yang C, He M, Zhang L. Screening for diabetic retinopathy in diabetic patients with amygdala-Free full-field flicker electroretinogram recording device. *Documenta Ophthalmologica*. 2019 Nov 12:1-9.

Pupil responses become attenuated as diabetic retinopathy gets worse



- 1992 Smith & Smith; Straub, Jeron, & Kerp
- 1994 Straub, Thies, Jeron, Palitzsch, & Scholmerich
- 2001 Nakayama et al.
- 2013 Ortube et al.
- 2016 Maa et al.
- 2020 Brigell et al.

Combining ERG with pupillary analysis may be a powerful predictor of diabetic retinopathy

1. Best eye's ERG implicit time
 - How long it takes the retina to respond
2. Best eye's ERG amplitude
 - How strong the signal is from the retina
3. Worst eye's pupil response
 - Change in pupil area from dim to bright light
4. Age

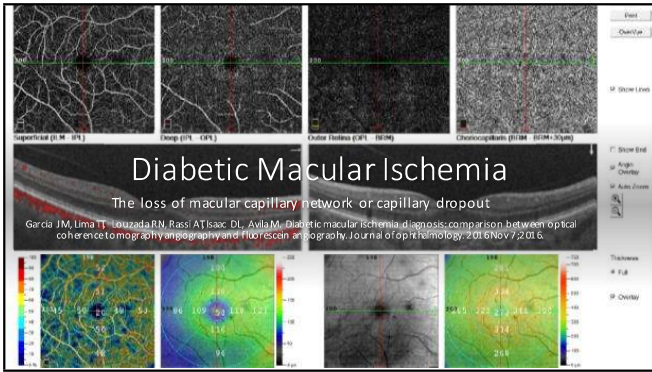
ERG DR Score

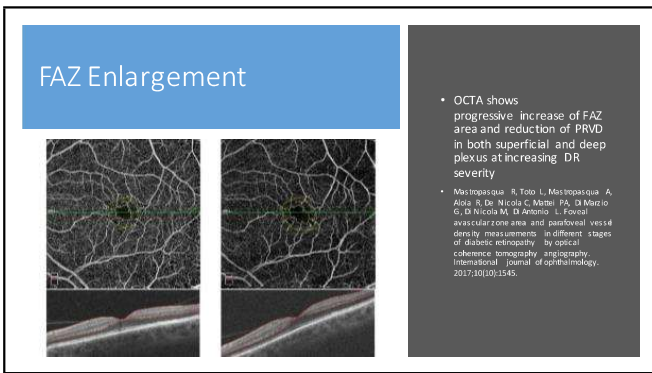
- William Feuer, MS
 - CIGTS
 - OHTS
 - Tube v Trab
 - Ahmed Baerveldt Comparison Trial
 - Leber's Biostatistics Center

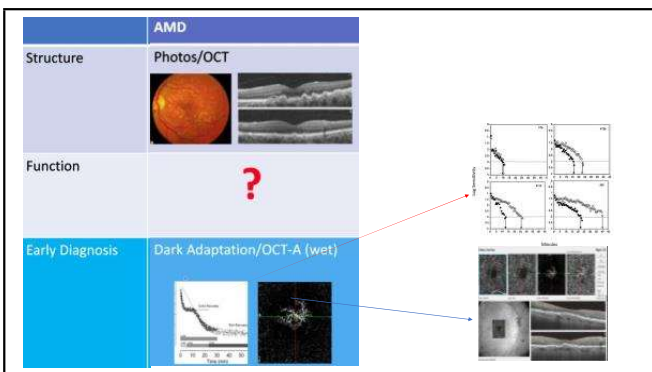
Combining Diabetic Structure and Function

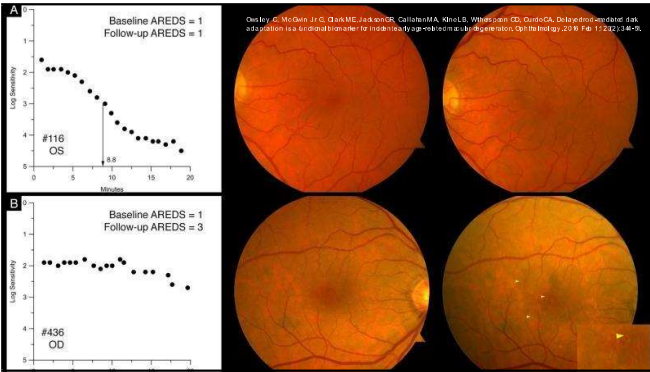
- VTDR+ = positive vision threatening diabetic retinopathy
- VTDR+
 - Severe NPDR
 - Proliferative DR
 - ME
- If patient had VTDR+, the chance of ocular intervention at 1, 2 and 3 years were **19%, 31%, 53%**
- If VTDR+ patient had ERG DR score greater than 23.5, chance of ocular intervention was **34%, 54%, 74%**
- If VTDR+ patient had ERG score less than 23.5, the chance of ocular intervention was **3%, 4%, 23%**

Bigell WG, Chiang B, MwaAV, Davis CO. Enhancing risk assessment in patients with diabetic retinopathy by combining measures of retinal function and structure. Translational vision science & technology 2020;Aug 3:9(9):40.







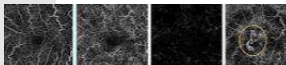



Recent Systematic Literature Review

- This systematic review indicates **overwhelming** evidence of reasonable quality for an association between impaired DA and AMD
- Data on the repeatability and reproducibility of DA measurement are sparse
- Higgins BE, Taylor DJ, Binns AM, Crab D.P. Are current methods of measuring dark adaptation effective in detecting the onset and progression of age-related macular degeneration? A systematic literature review. *Ophthalmology and therapy*. 2021 Feb 9:1-8.

OCT-A shows SRNV in AMD

- Can differentiate between SRNV type 1 and 2
 - Type 1
 - New vessels located **BELOW** RPE and **ABOVE** Bruch's membrane
 - Type 2
 - New vessels located **ABOVE** the RPE and **ABOVE** Bruch's membrane

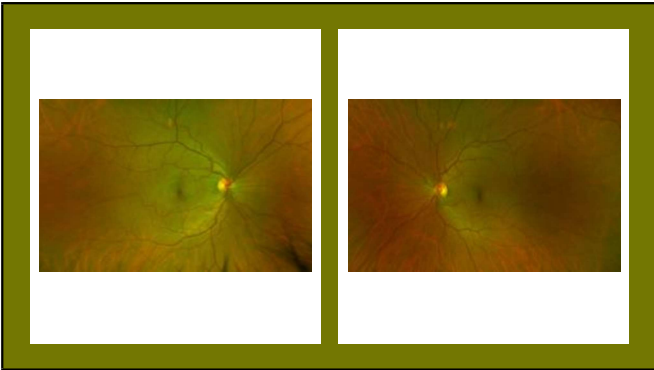



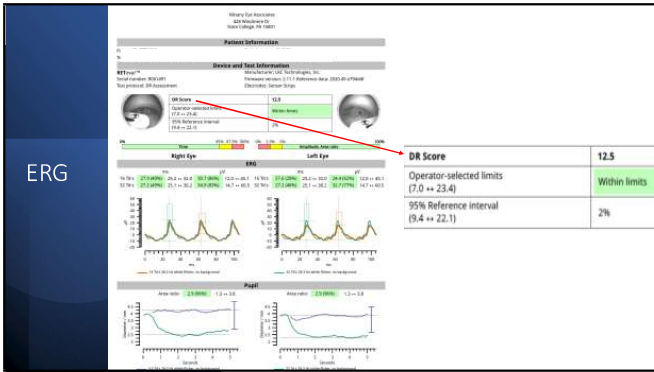
Muller J, Dorst M, Neugebauer G, Bittel A, Seifried D. Dark adaptation in retinal degenerative diseases. *Ophthalmology*. 2017 Feb 1;124:238-46.

Billing/Coding		
Description	CPT Code	Average Medicare Reimbursement
ERG with interpretation and report	92273	\$133
Dark adaptation with interpretation and report	92284	\$61
OCT with interpretation and report	92134	\$41

Case

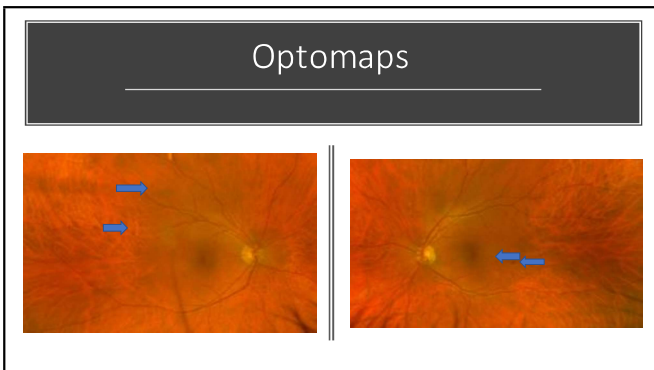
- 46 Y/O W/F
- Type 2 Diabetes x 5 years, HTN x 5 years
 - Metformin
 - Last A1C 6.8

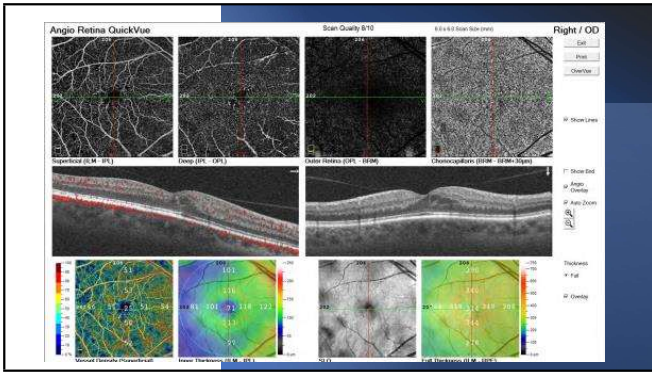


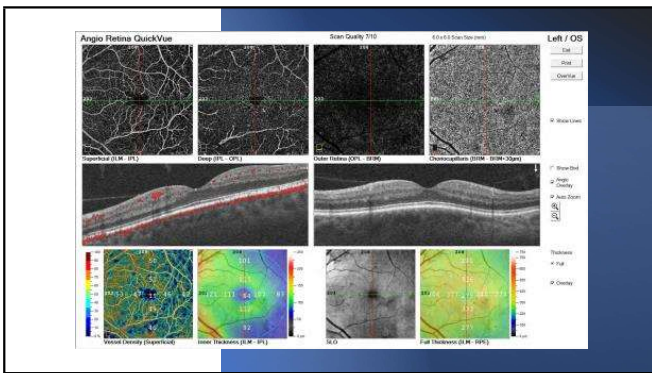


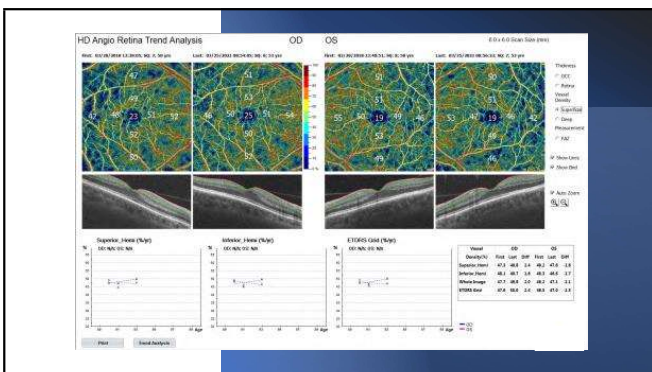
Case

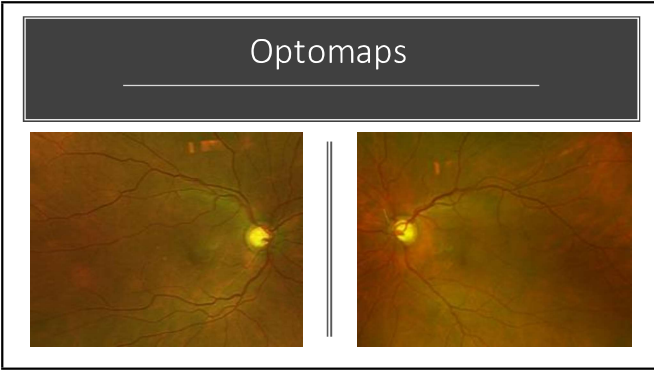
- 53 Y/O W/M
- Type 1 Diabetes x 20 years, Hypercholesterolemia x 3 years
- Mild non-proliferative diabetic retinopathy x 5 years
- Last HA1c 6.9
- BCVA 20/20 OD and OS





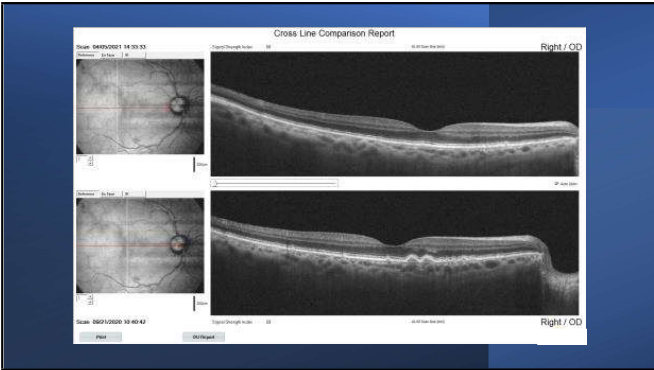




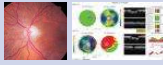
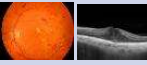
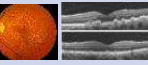

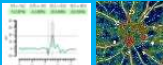
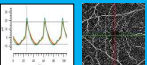
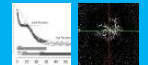


And now...

- 6 months ago, began new supplement, reports excellent compliance
- Adapt Dx 12.1 (Baseline 13.2)



Three Ocular Disease States

	Glaucoma	Diabetic Retinopathy	AMD
Structure	Photos/OCT 	Photos/OCT 	Photos/OCT 
Function	Visual Fields 	?	?
Early Diagnosis	ERG/OCT-A 	ERG/OCT-A 	Dark Adaptation/OCT-A (wet) 

Thank You



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