

Diabetic Retinopathy Grand Rounds: Interpreting ERG Findings

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Disclosures

Dr. Wood:

- **LKC Technologies** – Clinical Advisory Board
- **Alcon** – Contact Lens KOL/Speaker
- **Bausch & Lomb** – Contact Lens Expert/Speaker
- **Essilor Instruments** – LLLT/IPL Speaker
- **Euclid Vision Group** – Speaker/Consultant
- **Orasis Pharmaceuticals** – Speaker/Consultant
- **Pure & Clean** – Research/Speaker
- **Vision Source Administrator** – San Antonio
- **Vision Source Vendor Relations Consultant** – Equipment/Contact Lens

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DIABETES IN THE U.S

A SNAPSHOT

DIABETES

37 Million
37 million people have diabetes

That's about **1 in every 10** people

1 in 5 people don't know they have it

Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/diabetes/library/socialmedia/infographics.html>

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The Growing Threat of Prediabetes

96 Million
96 million American adults—more than **1 in 3**—have prediabetes

More than 8 in 10 adults with prediabetes don't know they have it

Pre-diabetes increases the risk of cardiovascular disease equally to overt type 2 diabetes

Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/diabetes/library/socialmedia/infographics.html>

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Prevalence of Diabetes

- One-third of Americans are at risk of developing diabetes mellitus^{1,2}
- Increasing prevalence is leading to a worldwide epidemic^{1,3}

The US Public Health System Relies on Optometrists to Diagnose and Help Manage These Patients

1. American Academy of Ophthalmology. Diabetic Retinopathy Preferred Practice Pattern. 2019. Published by Elsevier Inc.
 2. Narayan KM, Boyle JP, Thompson TL, Sorensen SW, Williamson DF. Lifetime risk for diabetes mellitus in the United States. JAMA. 2003;290(14):1884-1890.
 3. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet. 2011;378(9785):31-40.

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Prevalence of Diabetes


- 100 million Americans >18 have diabetes or prediabetes¹
 - 37.3 million Americans >18 have diabetes²
 - About one-quarter are not aware that they have the disease³
- Rates of prediabetes are increasing⁴
 - Nearly half (48.3%) of adults 65 or older have prediabetes²

1. American Academy of Ophthalmology. Diabetic Retinopathy Preferred Practice Pattern. 2019. Published by Elsevier Inc.
 2. Centers for Disease Control and Prevention. National diabetes statistics report, 2017. Available at: <https://www.cdc.gov/diabetes/pdf/data/statistics/national-diabetes-statistics-report.pdf>. Accessed September 2019.
 3. Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health And Nutrition Examination Survey 1999-2002. Diabetes Care. 2006;29(6):1263-1268.
 4. Diagnosing Diabetes and Learning about Prediabetes. 2014; <http://www.diabetes.org/diabetes-basics/diagnosis/>. Accessed September 2019.

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Structural Testing

Structural assessment for diabetic retinopathy should consist of ... UltraWide Field Retinal Screening/Photo



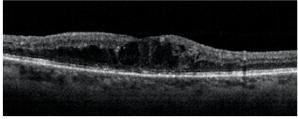
Examination of the retinal mid-periphery and/or Wide-field or ultrawide-field retinal imaging, when possible

Considering **peripheral DR lesions increases level of DR severity in ~10% of cases (DRCR Protocol AA)**

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Structural Testing

Structural assessment for diabetic retinopathy should consist of ... OCT of Macula



Spectral domain optical coherence tomography (SD-OCT) when any DR is detected to assess for DME

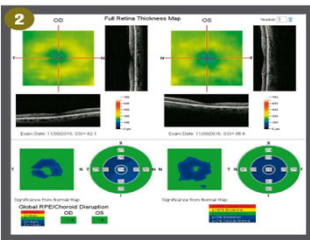
Also consider at baseline for future comparison



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Structural Testing

Structural assessment for diabetic retinopathy should consist of ... OCT



SD-OCT on patients with diabetes mellitus duration > 5-10 years to assess for **Retinal Diabetic Neuropathy** (RDN – defined as abnormal thinning of the retinal nerve fiber layer [RNFL] and ganglion cell complex [GCC] that portends functional vision loss and autonomic neuropathy)¹

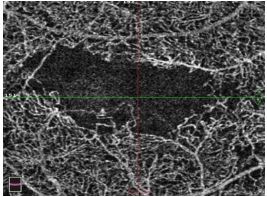
Recent analysis shows significantly increased risk of **MI, stroke, CHF** and all-cause **mortality** with inner retinal thinning²

1. *PLoS One*. 2017 Mar 23;12(3):e0174377.
2. *JAMA Neurol Open*. 2023 May 1;6(5):e2313220.

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Structural Testing

Structural assessment for diabetic retinopathy MIGHT also include ... OCT-Angiography



OCTA at baseline exam for future comparison to assess degree of retinal non-perfusion and presence of foveal ischemia

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Functional Testing Overview

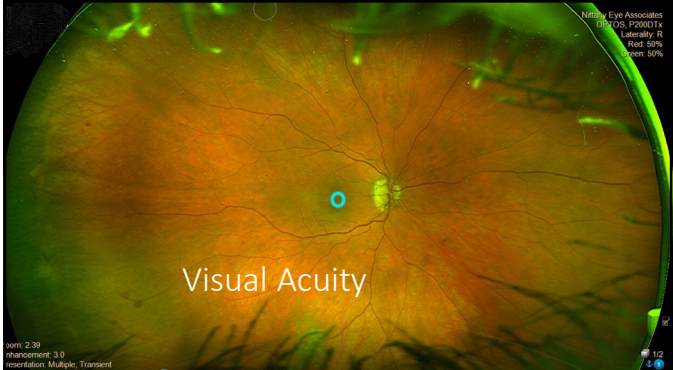
Standard of care for the assessment of vision loss due to diabetic retinopathy is high-contrast visual acuity, but evidence shows it is insufficient

- VA is subjective, unlike our structural tests
- VA only gives us an idea of the functioning of the fovea and perifoveal area
- VA often shows changes in visual functioning late in the disease process

But what do we NEED?

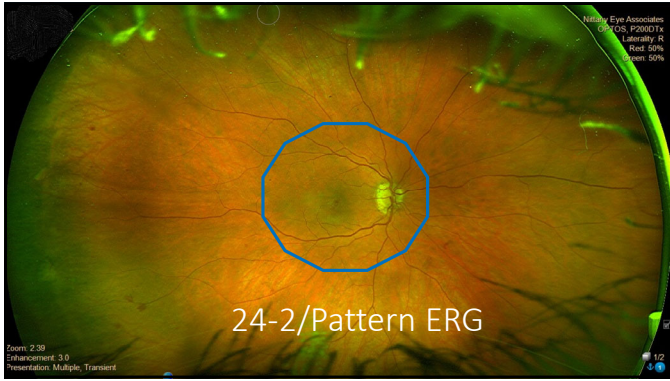
- Visual Acuity!
- Contrast Sensitivity?
- Color Contrast Testing?
- Visual Field Testing?
- Amsler Grid?
- Preferential Hyperacuity Perimetry?
- Dark Adaptation Testing?
- Electroretinogram (ERG)?

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Visual Acuity

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ERG 101

The Fundamentals of Functional Testing

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Electroretinography 101

ERG measures the electrical responses of various cell types in the retina, including the photoreceptors (rods and cones), inner retinal cells (bipolar and amacrine cells), and the ganglion cells in response to a stimulus.

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Types of ERG

- Full-field ERG (ffERG)**
 - Electrodes record the summed electrical response of the retinal cells
 - Shows the status of the retina as a whole
- Pattern ERG (PERG)**
 - Evokes electrical responses from the ganglion cells composing the inner retina
 - Used as a test for disorders affecting ganglion cells and neurodegenerative disorders
- Multifocal ERG (mfERG)**
 - Best for measuring dysfunction of the central retina area
 - Not sensitive to abnormalities in the ganglion axon

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Three Components of Full-Field ERG

- Amplitudes** are how far the baseline electric potential of the eye dips in the a-wave and climbs in the b-wave.
- Implicit times** are how much time elapses after the light flash until the trough of the a-wave or the peak of the b-wave.
- The **PhNR** originates from the activity of the retinal ganglion cells, the innermost cells of the retina that transmit signals to the brain via the optic nerve.

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.

A delay in **implicit times** indicates cellular stress / abnormal metabolism

Reduced **amplitude** indicates cells are dying, number of cells is decreasing

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Correlate Structure and Function

First published in 1987, results replicated in North & South America, Europe, and Asia

Increasing Disease Severity →

Zeng et al. (2019) "Screening for Diabetic Retinopathy in Diabetic Patients with a Mydriasis-Free, Full-Field Flicker Electroretinogram Recording Device". Documenta Ophthalmologica.

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Function: Assess Risk

DR Score Predicts Who Will Need Tx

Risk of Progression

Criterion	12-Month Progression Risk
RETeval DR Score ≥ 26.9	79%
RETeval DR Score ≥ 23.5	60%
OCT-A FAZ area $\geq 0.295\text{mm}^2$	53%
Fundus photography DRSS ≥ 47	42%
UWF-FA total ischemia index ≥ 0.125	41%

*49% of patients with a RETeval DR Score ≥ 26.9 or higher progressed to needing treatment within 6 months.

Davis, C. Quentin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859
Data found in Supplemental Figure 3, available online.

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Function: Assess Risk

DR Score Predicts Who Will Progress PDR/DME

Patients with a DR Score of 26.9 or higher had a 79% chance of progressing to needing treatment in less than 1 year.

- Longitudinal prospective study published in *Ophthalmology Science*, the journal of the American Academy of Ophthalmology
- 48 weeks (~11 months)
- 74 patients with moderate to severe NPDR tested with ERG
- Evaluated 56 parameters at multiple US sites from 4 testing modalities:
 - RETeval DR Assessment (ERG + pupillometry)
 - Color fundus photography (FP)
 - OCT angiography (OCT-A)
 - Ultra-widefield fluorescein angiography (UWF-FA)

Davis, C. Quentin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859

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Function: Assess Risk

Each 1-point change in the DR Score increases the probability of ocular intervention over 3 years by 28%

Higher DR Score & change over time dramatically increases risk:

- Risk of intervention **doubles** with a 3-point increase in DR Score (e.g. 20 to 23)
- Risk of intervention **triples** with a 4.5-point increase in DR Score (e.g. 20 to 24.5)
- Risk of intervention **increases 5x** with a 6.5-point increase in DR Score (e.g. 20 to 26.5)
- Risk of intervention **increases 12x** with a 10-point increase in DR Score (e.g. 16 to 26)

Increase in DR Score	Increase in Relative Risk of Intervention
3	2x
4.5	3x
6.5	5x
10	12x

Cox proportional hazards analysis (CI = 1.17 - 1.40, p < 0.0001)
Source: Briggall MC, Chang B, Miao A, Davis CC. Emerging Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. Trans Vis Sci Tech. 2020;9(9):46-49

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Predictive Value of Combining Diagnostic Technologies

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Case Report: Combining Structure & Function

- 39-year-old Caucasian male with type 1 diabetes mellitus (T1DM) x 18 years
- Basal/bolus insulin therapy via insulin pump
- Recent HbA1c = 6.4%
- History of HbA1c ranging from 6.4% to 12.7%
- Wears continuous glucose monitor (CGM) with 90-day time-in-range (TIR) = 64%
- Systemic medications:
 - Insulin aspart (NovologTM): 60-80 units daily
 - Levothyroxine: 150 mcg (Hashimoto's thyroiditis)

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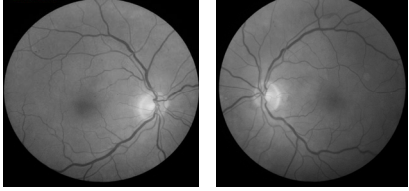
Ocular History

- Mild NPDR (scattered microaneurysms) at baseline (November 2023)
- Relevant family ocular history: POAG, maternal grandmother
- Ocular medications, procedures, surgeries:
 - NONE

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Fundus Exam

- Scattered ma OD/OS
- No VB/IRMA
- No NVD/NVE
- No DME



- BCVA: 20/20 OD/OS
- IOP: 16/17 mm Hg

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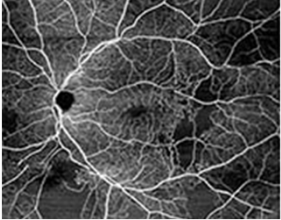
spOCT - Normal



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OCT-A

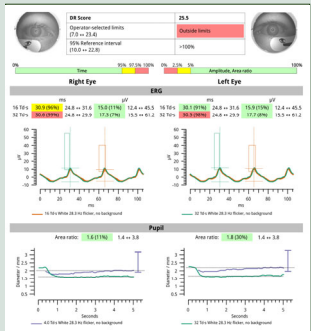
- Patchy areas of non-perfusion
- Irregular foveal avascular zone
- No evidence of IRMA/PDR



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ERG

- Abnormal DR Score (25.5)
- High risk of requiring a retinal intervention in the next 36 mos.
- ffERG + pupillometry performed for baseline and assessment of progression risk
- B-wave amplitude is at the lower end of the normal range (uv)
- Reduced implicit times (ms) OD > OS
 - Retinal stress




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How to Interpret the DR Score

PATIENT TEST CONDITIONS
Test is always done un-dilated. Patient is diabetic with suspected retinopathy or diabetic with existing retinopathy.

PROTOCOL
DR Assessment

RESULTS
If the Operator-selected limit is marked red with text **Outside limits**, the patient is at risk to develop vision threatening DR within the coming 36 months.



DR Score	6-Month Progression Risk	1-Year Progression Risk
19.9 or less	0%	0%
20.0 - 23.4	9%	48%
23.5 - 26.8	35%	60%
26.9 or greater	49%	79%

Davis, C. Quenlin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859

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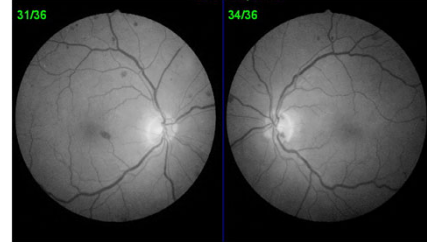
Follow-up

- Patient recalled sooner than he would have been based on fundus examination alone
 - Mild NPDR without DME
 - Abnormal DR Score (reduced retinal function)
 - Abnormal OCTA (areas of non-perfusion)
- Re-appointed x 4 months

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Follow-up Color Fundus Photography

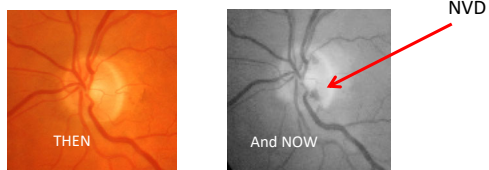
March 2024 images – rapidly worsening diabetic retinopathy



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Follow-up Color Fundus Photography

March 2024 images showing NVD OS



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Vision Complaints Reflected on **ERG**

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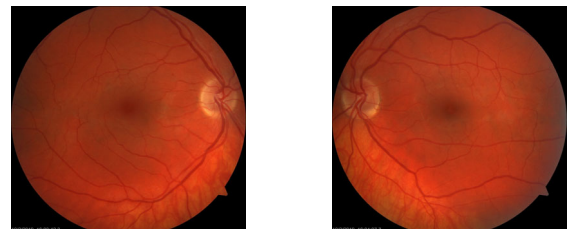
History

- 77-year-old male
- VA
 - 20/20-3 OD
 - 20/30+2 OS
- Type 2 DM x 19 years
 - Controlled with oral meds
 - Last A1C = 8.2

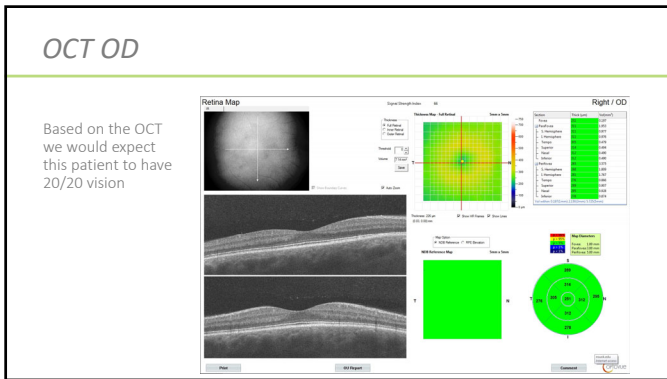
41

Fundus Exam

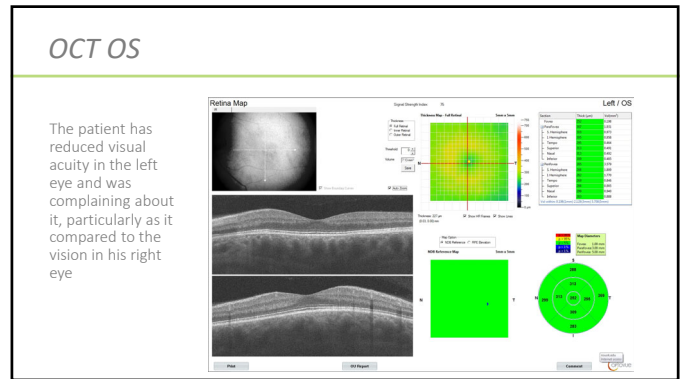
Mild non-proliferative diabetic retinopathy OD, with a small microaneurysm



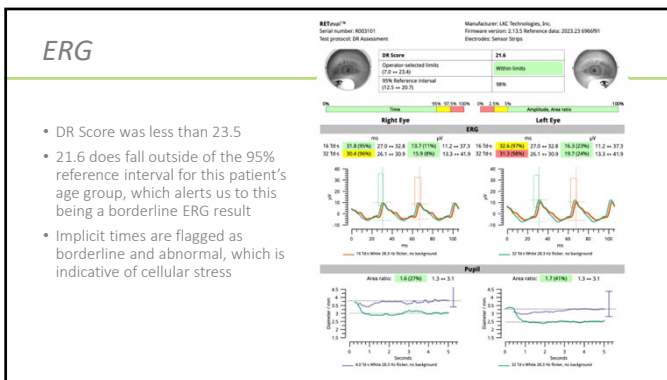
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Treatment

Discussed the impact of better nutrition

- Not motivated to change diet
- Disappointed with his vision
- Amenable to taking a supplement for retinal health

Follow-up at six months and one year

- Patient was using the supplement regularly
- A1C and diet remained unchanged

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One of those mornings:
Two DR Patients Appear to Require Identical Follow-up

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Patient 1

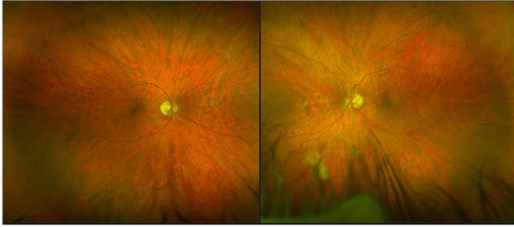
February 2024

- 63-year-old male
- Glaucoma suspect
- History of DR with macular edema
- Diabetes diagnosed age 37
- HgbA1c 6.0
- BCVA stable: 20/20 OD 20/25 OS
- Worsening dry eye symptoms
- Presented as instructed for follow-up
 - Diabetic retinopathy and glaucoma suspect
- History of mild diabetic retinopathy with macular edema
 - Managed by observation/treatment required

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Patient 1: Fundus Exam

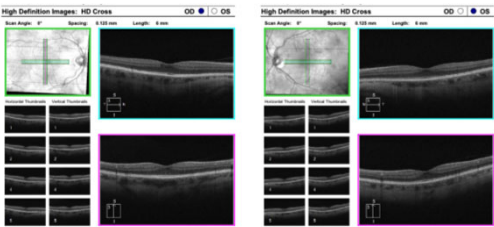
Dilated retinal exam showed few dot hemes OU



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Patient 1: OCT

Stable macular edema OD / No macular edema OS / Mild DR OU



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Patient 2

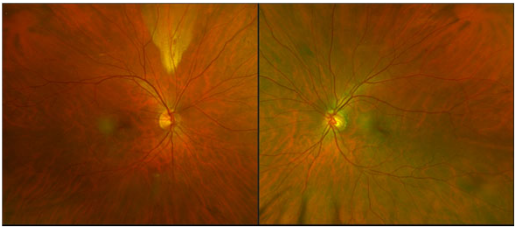
February 2024 (Same Day as Patient 1)

- 55 yo male
- Diabetes diagnosed age 37
- History of mild diabetic retinopathy without macular edema
- HgbA1c 9.1
- Presented for follow up for DR, has not noticed any changes in vision
- BCVA 20/20 OD 20/25 OS

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Patient 2: Fundus Exam

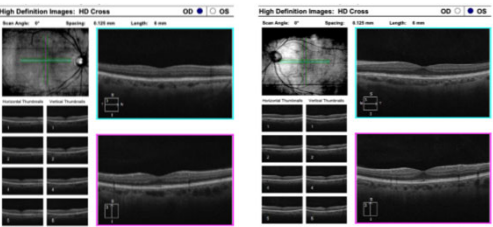
Dilated retinal exam showed scattered dot and blot hemorrhages OU.
 There is an area of myelinated NFL superior OD that has hemes within the myelination
 There are several dot hemes in the macula of each eye.



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Patient 2: OCT

Normal OD / Mild cystic changes OS (early macular edema)



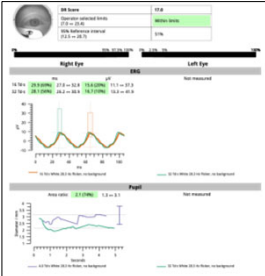
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The ERG Difference: Why These Patients Need Different Follow-up

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Patient 1: ERG

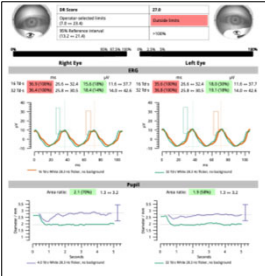
- DR Score 17
- May explain why this patient has had macular edema for 3 years but has not progressed to needing treatment
- Follow up 6 months
- Having the ERG on this patient that did not show high risk for conversion to severe retinopathy made me comfortable with the plan for a 6 month follow up instead of more frequent



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Patient 2: ERG

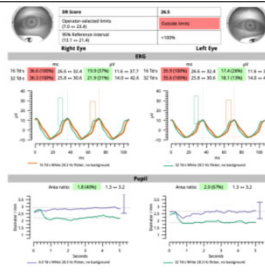
- DR Score: 27
- Follow up 3 months



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Patient 2: Three-Month Follow-up

- No vision changes, following up as instructed
- HgbA1c 9.6
- ERG DR score 26.5
- OCT normal OD, slight improvement in macular edema OS
- Next visit 3 months
- Due to the higher DR score on ERG, I have continued to follow this patient every 3 months instead of every 6



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Key Takeaways

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How often do you see these patients?

Diabetic retinopathy	Glaucomatous optic atrophy	Changes in retinal vascular appearance	Central serous chorioretinopathy	Disorders of the optic nerve & visual pathway	Drusen of optic disc
Epiretinal membranes/puckering of the macula	Hypertensive retinopathy	Multiple defects of the retina without detachment	Nonequidative age-related macular degeneration	Nystagmus	Central retinal vein occlusion (CRVO)
Optic neuritis	Other specified retinal disorders	Other visual disturbance	Papilledema	Peripheral retinal degeneration	Retinal detachment with retinal break
Retinal hemorrhage	Retinal microaneurysms	Unspecified night blindness	Unspecified visual disturbance	Venous engorgement	Exudative age-related macular degeneration

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My "Must-Have" Functional Test

OBJECTIVE

- ERG tests are successful without patient cooperation and cognitive understanding
- Patient cannot influence results, neither can eye opacities

PREDICTIVE

- ERG tests have a high predictive value as a tool for diagnosing
- Ischemic changes can be detected even three years prior to their appearance on other devices

FUNCTIONAL

- Structure matters, but function is the other piece of the puzzle
- Collecting data from both gives you the full picture to make clinical decisions

REIMBURSABLE

- Reimbursable with CPT code 92273

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Additional Slides

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A Global DR Score Predicts Who Will Need Tx

- N = 237 in US
- Primary outcome: % receiving laser, IV therapy and/or vitrectomy over 3 yrs
- Clinically observable SEVERE NPDR in tandem with ERG+pupillometry score > 23.5 best predicted Tx

ERG/Structural Signs	% Patients Needing Treatment in 3 Years
RETeval <23.5 & No Structural Signs	6%
RETeval <23.5 & Structural Signs	18%
RETeval >23.5 & No Structural Signs	20%
RETeval >23.5 & Structural Signs	67%

Brigell MS, Chang B, Mao AY, Davis CO. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. Trans Vis Sci Tech. 2020;9(9):40-46.

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Case Report 3: Abnormal ERG motivates PCP/Patient

49 yo Hispanic Female, New Patient
T2DM, Hypertension, NO Hx of NPDR OU.
Last HbA1c 7.5, 3mo prior 8.0, 6mo prior 9.0
Meds: Ozempic, Atenolol (has lost 30 lbs last 6mo)
Reason For Visit: Referred by PCP for Diabetic Eye Exam
BCVA: OD: 20/25 OS: 20/30
Biomicroscopy: Unremarkable OU
IOP (iCare): OD: 12mm Hg OS: 14mmHg

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Case Report 3: Abnormal ERG motivates PCP/Patient

OD Evaluation:

DFE/Fundus Photo:

- Dot hemes 2 quads
- Hard exudate posterior pole & mid periphery

OCT Macula:

- CMT 262um
- (-) DME
- (+) Non-Central Retinal Edema

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Case Report 3: Abnormal ERG motivates PCP/Patient

OS Evaluation:

DFE/Fundus Photo:

- Dot hemes 1 quad
- Mild exudate posterior pole

OCT Macula:

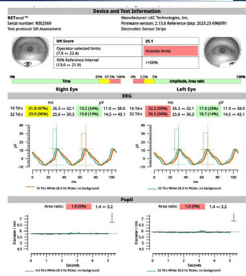
- CMT 263um
- (-) DME
- (+) Non-Central Retinal Edema

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Case Report 3: Abnormal ERG motivates PCP/Patient

- DR Score** **3.4 (Abnormal)**
 - (high risk SX intervention 3 yrs)
- Implicit Time**
 - OD: **Borderline** photoreceptor cellular stress
 - OS: **Abnormal** photoreceptor cellular stress
- Amplitude**
 - OU: Normal (good volume of PR cells remain)
- Pupil Motility**
 - Abnormal** (pupil ischemia)

CONCLUSION:
History of poor T2DM control causing cellular stress of photoreceptors.
Good Amplitude so Good Prognosis for improvement



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Case Report 3: Abnormal ERG motivates PCP/Patient

3 month Diabetic Retinopathy Follow Up Evaluation

- Last HbA1c: **6.6**, 3mo prior **7.5**, 6mo prior **9.0**, 9mo prior **10.0**
- Meds: **Ozempic**, Atenolol (**has lost 35 lbs last 9mo**)
- BCVA: OD: **20/20-1 (improved)** OS: **20/25 (improved)**
- Biomicroscopy: Unremarkable OU
- IOP (iCare): OD: 17mm Hg OS: 18mmHg

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Case Report 3: Abnormal ERG motivates PCP/Patient

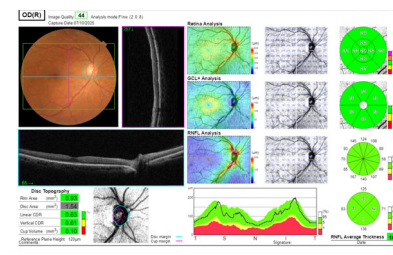
OD Evaluation:

DFE/Fundus Photo:

- Dot hemes 1 quad **(improved)**
- Hard exudate **(improved)**

OCT Macula:

- CMT 254um **(improved)**
- (-) DME **(stable)**
- (+) Non-Central Retinal Edema **(improved)**



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Case Report 3: Abnormal ERG motivates PCP/Patient

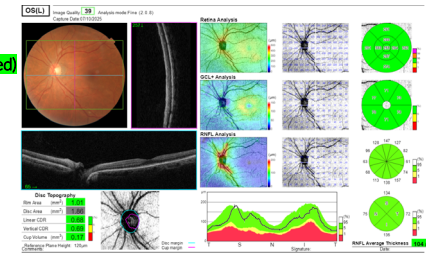
OS Evaluation:

DFE/Fundus Photo:

- Dot hemes 1 quad **(improved)**
- Hard exudate **(improved)**

OCT Macula:

- CMT 259um **(improved)**
- (-) DME **(stable)**
- (+) Non-Central Retinal Edema **(improved)**

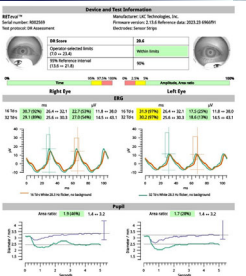


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Case Report 3: Abnormal ERG motivates PCP/Patient

- DR Score** **10.6 (Normal/Improved)**
 - (LOW risk SX intervention 3 yrs)
- Implicit Time**
 - OD: **Normal** No PR cellular stress **(improved)**
 - OS: **Borderline** PR cellular stress **(improved)**
- Amplitude**
 - OU: **Normal** (good volume of PR cells remain)
- Pupil Motility**
 - Normal OU **(improved)**

CONCLUSION:
Improved/Normal DR Score with improved HbA1c and T2DM management. Risk of progression needing Sx intervention LOW at current status.



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DR Management Fundamentals: Functional Testing

RETeval[®]
EXCITING ANNOUNCEMENT
ERG Named in Diabetic Retinopathy Preferred Practice Pattern Update



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THANK YOU!

Questions?

Bobby "Chip" Wood, Jr., OD
bwood@visionsource.com