Putting the "Oh!"in OCT

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Disclosures

FERRUCCI

- Apellis
- I-care/Centervue
- Iveric
- Notal Vision
- Novartis
- Optovue
- Science Based Health
- Visible Genomics

YACKEY

- Notal Vision
- Iveric Bio
- Reliance
- Novartis
- OcuTerra

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What is OCT?

- OCT =Optical Coherence Tomography
- Noninvasive, noncontact, laser-based technology that evaluates the reflectivity of light in semi-transparent materials (ocular tissues)
- Similar to how radar or ultrasound uses sound waves to provide information about density and spatial orientation
- Light waves are faster and shorter wavelength than sound – greater resolution and speed of capture

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Why is OCT Suitable for Retinal Imaging?

- The internal structures of the eye and the retina are optically clear, except in states of disease
- The retina is organized in predictable, fixed layers circumferential and parallel to the eye wall
- The macula, the "focusing point" for vision, is also the fixation point of gaze and the area of interest for microanatomic study

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A-scan vs B-scan

- A-scan = "A" single scan
  - Provides information about a single pathway of light and the objects that interfere with that path as light is reflected back towards the sensor
- B-scan = "Bunches" of scans
  - Provides a 2-dimensional picture representation from several A-scans
  - Conventional representation for OCT

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OCT Technology: Advantages

- Has ushered in a whole new era of retinal care
  - Diagnosis
  - Response to treatment
- New diagnoses once only speculated
  - VMT
  - Macular Schisis
- Can replace FA in many cases

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OCT Technology: Caveats

- DOES NOT take place of clinical exam!
- DOES NOT take place of careful history taking
- DOES NOT replace FA in some cases!
- DOES NOT REPLACE COMMON SENSE!

- ONE MORE PIECE OF CLINICAL PICTURE
  - Not the end all be all!!
  - Not to be taken in vacuum

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Common Types of Vitreoretinal Pathology by Anatomic Location

- Retinal Surface - Vitreous and ILM
- Inner Retina
- Outer Retina/RPE/Choroid

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Vitreous

- Collagen and hyaluronic acid gel matrix congenitally adherent to the retina and optic nerve
- Degrades over decades as gel matrix dehydrates and coalesced fluid pockets forms, ultimately resulting in separation of the vitreous from the posterior retina and optic nerve (posterior vitreous separation)
  - Accelerated by trauma, inflammation, hemorrhage, myopia, ocular surgery, degenerative retinal diseases
- Vitreous separation is a discrete window when retinal tears or retinal detachment typically occur (15% risk in general population)

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Vitreous Attachment/Detachment

- Vitreous consistency is like epoxy glue (sticky and stringy more than gooey)
- Pathologic states involve abnormal excessive adhesion between gel and retina
- Symptomatic retinal breaks usually accompany PVD
- Completion of PVD significantly reduces risk for future retinal breaks
- Surgical approach for RD repair depends on PVD status

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Vitreoschisis

- The vitreous gel is arranged in layers, like skins of an onion
- The layers closest to the innermost layer of the retina (ILM) are tightly adherent and may strip away from the vitreous body in pathologic states

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Vitreomacular Traction Syndrome

- Aka "Vitreomacular adhesion"
- Partial macular vitreous separation with anomalous foveal adherence, creating schisis (splitting)
- Analogous to ripping wires of an electrical system apart, which reduces function
- Chief complaints:
  - metamorphopsia
  - scotoma

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VMT

- More commonly encountered in older women
  - Can occur in either sex, and age, no apparent racial predilection
- Aphakia and pseudophakia are protective
- VAST STUDY
- 2,179 eyes, 1,120 asymptomatic pts>40 years of age
  - Mean age 59
  - 57% female
  - 57% hyperopes, 35% myopes, 8% emmetropes
- VMA in 31% of eyes
  - Peak age 50-59
  - Less common in AA and HA

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VMT

- Natural progression of disease is rather variable
  - Slow progression possible with near normal acuity
  - Approx 10% will have spontaneous PVD and resolution AT 30 DAYS
  - Approx 30% will resolve after 90 days
- In patients with poor vision, or symptomatic, a pars planar vitrectomy (PPV) may be considered
  - Duration, severity should also be considered
- Literature reports up to a 75% success rate and improvement of vision following PPV

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Diabetic Tractional Retinal Detachment

- Proliferative (neovascular) diabetic retinopathy thickens/toughens the ILM-vitreous interface (adhesion) while prematurely aging the vitreous body (contraction)
- Degree of tractional forces depends on quantity (more) and quality (fibrotic) of new vessels

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Full Thickness Macular Hole

- More severe form of VMT resulting in full thickness foveal defect
- Stages:
  1 = outer retinal defect
  2 = full thickness defect with vitreous traction on one edge
  3 = operculum
  4 = PVD
- Chief complaint: **scotoma**
- Treatment: Surgery, Intravitreal Ocriplasmin

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FTMH

- Definition: Macular hole that affects all macular layers from ILM to RPE
  - vs lamellar or partial
- Vision typically 20/80 to 20/200
- Highest incidence in 7th decade of life
- Women 2x as often as men
- If pt has macular hole in one eye, 28-44% chance of macular hole in other eye w/o a PVD
  - If PVD already, very little chance
- Most common cause is idiopathic or "primary"
  - With advent of OCT realize "idiopathic" is due to vitreoretinal traction
  - Secondary causes include blunt trauma, severe myopia, solar retinopathy, CME

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FTMH

- Small holes: <250 um
  - Small rate of spontaneous closure
  - Very high surgical closure rate (almost 100%)
- Medium holes: 250um to 400um
  - High surgical closure rate (>90%)
- Large holes: >400 um
  - High surgical closure rate (75-90%)

½ of all holes are large at time of diagnosis

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Vitreous Opacities

- Opaque objects in the vitreous block the OCT's laser, producing **SHADOWING** of deeper layers
- Examples: Asteroid hyalosis (calcium), hemorrhage, inflammation, intraocular foreign bodies, vitreous opacities
- Treatment: Surgery

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Epiretinal Membrane

- Thickened mass of cells at the VR interface (hyaloid, reactive, RPE)
- Very common (25% after PVD), but most not visually significant
- Chief Complaints: **metamorphopsia, blurred vision**
- Treament: Surgical Removal

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Lamellar Macular Hole

- Symptoms
  - mild metamorphopsia
  - limited acuity loss
  - stable vision
- Surgery is controversial
  - 25% to 75% improved visual acuity
- Therefore, monitoring seems reasonable

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Myopic Macular Schisis

- Pathologic myopia disproportionately elongates posterior aspect of eye (egg-shaped)
- Posterior hyaloid face acts like ERM and contracts against excessive posterior curvature of myopic macula
- Results in splitting (schisis)

Staphyloma

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Retinal Detachment

- Contraction of vitreous body, often with PVD, can result in retinal tears if VR traction exceeds retinal integrity
- Retinal breaks become an avenue for subretinal fluid and overwhelm the RPE pump, creating RD
- Macular status determines urgency of repair and prognosis about visual outcome

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Inner Retina

- Responsible for processing light information from multiple photoreceptors and transmitting it through the optic nerve towards the brain
- Contains nerve fiber layer, ganglion cells; bipolar, amacrine, and horizontal cells; Müller cells
- The retina receives oxygen from two sources
  - Inner 2/3 supplied directly by retinal blood vessels
  - Outer 1/3 supplied by diffusion from the choroid
- Obstruction of the retinal circulation produces visible changes on OCT

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Retinal Artery Occlusion

- Acute obstruction of a retinal artery results in ischemia (dysfunction) and ultimately infarction (death)
- Acutely, inner retinal edema seen clinically as **retinal whitening**
- Chief complaint:
  - scotoma, blindness
- Treatment controversial: paracentesis, globe compression, YAG laser embolysis, aspirin
- Workup: R/O GCA, Carotids, Echo, Hypercoagulability workup, Vasculitis/Uveitis workup

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Retinal Vein Occlusion

- Venous obstruction releases contents of the bloodstream (water, blood cells, and cholesterol) into the retina
- Plumbing problem
- Chief Complaints: blurred vision, scotoma, metamorphopsia
- Treatment: manage underlying vascular disease (HTN, DM, OSA) and/or glaucomas, retinal lasers, intravitreal anti-VEGF and/or corticosteroids

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Diabetic Retinopathy
Diabetic Macular Edema

- Diabetes preferentially damages capillary beds, creating microaneurysms and avascular zones
- Clinically edema, exudates, and hemorrhage are seen in varying degrees associated with vascular anomalies
- Similar to RVO, intraretinal hyperreflective areas and inner and outer retinal cystic hyporeflective cavities are seen on OCT

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Macular Telangiectasia Type 2

- Idiopathic macular disease associated with
  - Retinal telangiectasia
  - Cystic macular degeneration
  - RPE hyperplasia
  - Intraretinal crystals

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Outer Retina/RPE/Choroid

- Outer Retina - retinal photoreceptors are highly specialized neurons that generate electrical responses to light.
- RPE – multipurpose layer needed to maintain outer retinal function and health
- Choroid – high flow blood vessel layer that sustains outer retina by diffusion

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Age-Related Macular Degeneration

- Most common cause of blindness in the US in adults over 50
- "Dry" = progressive loss of RPE/outer retinal function/cells (atrophy) with accumulation of drusen (hallmark lesion)
- "Wet" = development of new choroidal vessels outside the choroid that leak water, blood, or cholesterol into the subRPE or subretinal space
- Chief Complaints:
  - Blurred Vision
  - Metamorphopsia
  - Scotoma
- Treatment

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Drusen

- Accumulation of incompletely recycled visual cycle pigments that could not be returned to the photoreceptors in conjunction with complement cascade components/inflammatory debris
- Accumulate progressively, but distribution can fluctuate in some patients
- Loss of drusen frequently accompanied by RPE atrophy (geographic atrophy)

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CAM: Classification of Atrophy Meeting

- In addition to drusen and pigment changes in the fundus, we have learned of many other risk factors for developing GA in AMD.
- An international group of experts surveyed the existing literature, performed a masked analysis of longitudinal multimodal imaging for a series of eyes with AMD, and reviewed the results of this analysis to define areas of agreement and disagreement.
- Defined biomarkers and nomenclature in geographic atrophy
  - SD-OCT helps to identify and differentiate the atrophy as it progresses

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Hyperreflective Foci

- Punctate intraretinal lesions
- Often at drusen apex
- Likely represent pigment granules
- Originate in the outer retina and migrate inward with time
- 5 x more likely to form GA within two years

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Subretinal Drusen Deposits (SDD)

- AKA reticular pseudodrusen
- Difficult to distinguish from true drusen on color photography
- SD-OCT allows us to see the location as deposits in the subretinal space above RPE
- Early stage: granular hyperreflective deposit below EZ
- Progression is noted when material accumulates into small mounds that break the EZ.
- FAF: target shape with hypo- or isoautofluorescent surround. Collectively forms reticular pattern

Color Photo | Red-Free | Fundus Autofluorescence

SD OCT

SDDs = 2-6 x higher risk for GA

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Hypertransmission defects signify a high risk towards nascent GA.

Hypertransmission defects

- Increased hyperreflectivity in the choroid as a result of RPE disruption.
- The overlying RPE may "appear" intact and unaltered, however hypertransmission defects indicate loss of integrity of the RPE.

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VOCAB per the CAM group

Nascent GA/iRORA

- **Nascent GA**: "subsidence" or collapse of the outer plexiform layer (OPL) and inner nuclear layer (INL) and a hyporeflective wedge shaped band within the OPL.
- **iRORA**: the same definition as Nascent GA, but includes choroidal hypertransmission defect, signs of photoreceptor degeneration, and RPE attenuation/disruption.

cRORA

- Choroidal hypertransmission of 250 microns in diameter or greater
- A zone of attenuation or disruption of the RPE of at least 250 microns in diameter
- Evidence of overlying photoreceptor degeneration
  - ONL thinning, ELM loss, EZ or IZ loss
- All occur in the absence of signs of a RPE tear

*RORA=RPE and Outer Retinal Atrophy i=incomplete c=complete

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Choroidal Neovascularization

- A break in Bruch's membrane and/or RPE associated with leaky vessels
- Type 1: SubRPE
  - Wet AMD
- Type 2: Subretinal
  - Inflammatory
  - Pathologic Myopia
- Type 3: Retinal Angiomatous Proliferation
  - Wet AMD
  - Macular Telangiectasia

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Pathologic Myopia

- Axial myopia, commonly called "near-sightedness," in its extreme form
- Represents a connective tissue weakness
  - Elongates the eye, thinning the layers of the eye wall (cornea, sclera, choroid, RPE, retina)
  - Degenerating the vitreous early (collagen and hyaluronic acid)
  - Creating traction between the stretched retina and vitreous
  - Predisposes to vitreoretinal interface disorders, retinal tears, and retinal detachment

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Myopic Macular Degeneration

- Thinning of the posterior eye wall layers
- Increased posterior curvature (staphyloma)
  - Diffuse or focal
- RPE thinning/atrophy (lacquer cracks, geographic atrophy)

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Central Serous Retinopathy

- Vision typically 20/30—20/70
- Typically self-limiting
  - 80-90% of pts will undergo spontaneous resolution within 1-6 mos.
    - >60% resolve back to 20/20
    - Rare to have vision remain < 20/40
  - ≅40% will get recurrence
- FA is helpful in providing definitive diagnosis
  - Classic Smoke stack appearance (occasionally)
  - Ink-blot appearance
- Not needed with advent of OCT/OCTA unless unusual presentation

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CSR: Risk Factors

TRADITIONAL

- Male > Female 10:1
- Age: Peak 20-45
- Type A personality
- Stress
- Pregnancy

OTHERS

- Steroid use
  - Oral
  - Topical?
  - Inhaled?
  - Injection?
- Choroidal Thickness
- Sleep apnea?
- Genes?
- Viagra?

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CSR

- **When to worry/refer**
  - If VA worse than 20/70
  - If pt demographics do not support
  - If does not resolve in 6 mos
  - If gets worse rather than better
  - FA/ OCT does not support diagnosis
  - "Just doesn't feel right"
  - Pt is unable to accept vision/prognosis

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CSR: Treatment

- Observation
- PDT
- Anti-VEGF
- Anti-corticosteroids
  - Rifampin
  - Mifepristone
  - Ketoconazole
  - Spironolactone/eplerenone
  - Finasteride
- Acetazolamide
- Aspirin
- Metoprolol
- H.pylori treatment
- Methotrexate
- Behavior Modification!

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Photoreceptor Dystrophies

- The outer retina is dominated by photoreceptors, highly-specialized neurons that convert light information into electrical signals for the brain to process as vision
- Rods – dim light, peripheral vision
- Cones – bright light, color perception, visual acuity
- Chief complaints
  - Night blindness (nyctalopia)
  - Day blindness (hemeralopia)

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Role of Clinical History in Segregating Diagnoses

- Although some OCT findings are pathognomonic (i.e. macular hole), most need a chief complaint and limited history to add context and get the right treatment
- Specific visual complaints can help localize pathology
- Floaters – Vitreous
- Distortion – Retinal surface, intraretinal, or subretinal
- Distortion with scotoma – severe intraretinal or subretinal
- Scotoma – any layer except vitreous
- Amaurosis – inner retinal circulation

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Patient presents for AMD evaluation…

- 75 year old white woman
- CC: Patient moved from California to Ohio. New to the area, the patient states that she was diagnosed with Dry AMD by her eye doctor in California. Patient states that her vision has been decreasing for several years now. She is having difficulty seeing details and no longer reads. In general, she feels her vision is keeping her from doing what she loves to do. She no longer drives.
- Amsler grid testing: Irregular in both eyes with central metamorphopsia OU
- Pupils and slit lamp within normal limits OU

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Let's take a look at our patient's medication list…

- Centrum Complete
- Vitamin D3
- Sertraline HCl
- Lisinopril
- Levothyroxine Sodium
- Diclofenac Sodium
- Hydroxychloroquine (Plaquenil) 200mg BID

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What is Plaquenil (Hydroxychloroquine)

- A medication originally used to treat Malaria.
- Now used to treat a variety of autoimmune disorders and their symptoms.
  - Lupus
  - Rheumatoid Arthritis
  - Sjögren's Syndrome
- Plaquenil is used to treat skin disorders
  - Sarcoid, Eczema, Skin disorders where there is photosensitivity, Lichen Planus and Urticarial Vasculitis

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How Plaquenil works

- Lowering the immune system's ability to cause inflammation.
- Reduces inflammation
- Can help control symptoms:
  - Rash
  - Sores
  - Joint pain

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Possible Ocular Effects of Plaquenil (Hydroxychloroquine)

- A rare side effect of extended or over-dose Plaquenil use can be damaging, or toxic to the Retina.
- It is believed that Plaquenil binds itself to the Retinal Pigment Epithelium (RPE) and can cause damage to the photoreceptors.
- Typically asymptomatic in its early stages, but can lead to severe retinal damage, and permanent vision loss.
- Early signs include blurry central vision, losing the ability to read a digital clock, loss of color vision, and trouble seeing at night.

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Higher Risk Factors for Toxicity:

- Taking Plaquenil for 5+ years
- Taking a higher than recommended dose
- Pre-existing Kidney or Liver Disease
- Pre-existing Retinal Disease
- Age 60 or older
- Losing a significant amount of weight while taking Plaquenil without adjusting your dose
- May be more common than previously thought (≅7%)

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- The current American Academy of Ophthalmology (AAO) guidelines, published in 2016, recommend a maximum daily hydroxychloroquine dose of ≤5.0 mg/kg of real weight. These guidelines were established to minimize the likelihood of permanent vision loss related to hydroxychloroquine retinopathy.
- The 2016 revision was prompted by a study by Melles and Marmor in 2014 which suggested that hydroxychloroquine retinopathy is more common than previously thought. They demonstrated that a daily consumption of 5.0 mg/kg real body weight or less is associated with a low risk for up to 10 years. However, there is significant variability in individuals that develop hydroxychloroquine retinopathy.
- This study was performed only in adult patients.
- The American College of Rheumatology updated their guidelines in August 2016 to acknowledge the American Academy of Ophthalmology's position, but does not specify a preferred dosing regimen.
- Doses must be adjusted for renal insufficiency.
- Patients with underlying retinal or macular disease may be at a higher risk for toxicity.
- Patients who are undergoing tamoxifen therapy for breast cancer have a higher risk for toxicity.

mdcalc.com

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Important Exam Testing:

- HPI should include:
  - How long have you been taking Plaquenil?
  - What is your weight?
  - What is your dose?
  - Do you have a history of Kidney disease?
- Have you noticed any changes in your vision?
  - Baseline testing should be completed before, or within the first year of, beginning Plaquenil.
  - Testing:
    - 10-2 Humphrey Visual Field (HVF)
    - OCT Macula
    - Fundus Autofluorescence (AF/FAF)
    - Color vison

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