Retinal and OCT Grand Rounds

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Disclosure Statement

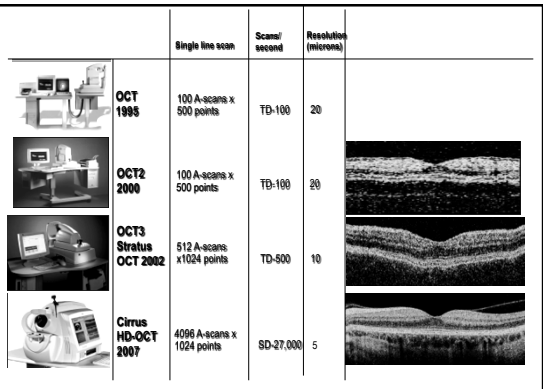
- **Speakers bureau/Advisory Board**
  - **Allergan**
  - **Alcon**
  - **AutoGenomics**
  - **B&L**
  - **Centervue**
  - **Heidelberg**
  - **Macula Risk**
  - **MacuLogix**
  - **Science Based Health**

Optical Coherence Tomography

Optical: Light-based

Coherence: property of light waves in which the oscillations maintain a fixed relationship to each other

Tomography: Cross-sectional imagery



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
- Information once only available through histopathology or dissection
- Can replace FA in some cases

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

Table 2. Chloroquine and Hydroxychloroquine Screening Procedures

Timeline	Baseline examination within first year of use Annual screening after 5 yrs of use
Recommended Screening Procedures	
Ocular examination	Dilated retinal examinations are important for detection of associated retinal disorders, but should *not* be relied on for screening (low sensitivity).
Automated visual field	White 10-2 threshold testing. Interpret with a low threshold for abnormality, and retest if abnormalities appear.
In addition, if available, perform one or more of the following objective tests	
SD-OCT	Rapid test that can be done routinely; can show abnormalities very early, even before field loss
mfERG	Valuable for evaluation of suspicious or unreliable visual field loss; may show damage earlier than visual field testing
FAF	May validate other measures of toxicity; can show abnormalities earlier than field loss
Not Recommended for Screening	
Fundus photography	Recommended for documentation, especially at baseline, but not sensitive for screening
Time-domain OCT	Insufficient resolution for screening
Fluorescein angiography	Use only if corroboration of pigmentary changes is needed
Full-field ERG	Important for evaluation of established toxicity, but not for screening
Amsler grid	Use only as adjunct test
Color testing	Use only as adjunct test
EOG	Questionable sensitivity

EOG = electro-oculogram; FAF = fundus autofluorescence; mfERG = multifocal electroretinogram; SD-OCT = spectral domain optical coherence tomography.

Impact of the guidelines on today's practice! AJO 8/2013

- n=183 pts came for f/u & 36 were evaluated for baseline
- Evaluated by 26 ophthalmologist & 3 ODs
- Results
  - 40% increase on health care cost
  - No additional pts discover with toxicity in accordance to new guideline.
  - Incidence of toxicity remains at 1%, as noted in f/u pts
  - No pts was followed at recommended guidelines of 5-year period after baseline (even if low-risk patient)

JAMA Ophthalmol. 2014 Dec;132(12):1453-60. doi: 10.1001/jamaophthalmol.2014.3459.

The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy.

Melles RB1, Marmor MF2.

- Retrospective study of 2361 pts who used plaquenil for at least 5 years
- Overall prevalence of maculopathy was 7.5%
  - 3 times noted in previous studies
- RISK factors:
  - Daily dose >5.0 mg/kg of real body weight
    - Previous 6.5 mg/kg of ideal body weight
  - Duration >10 years
  - Kidney disease
  - Concurrent tamoxifen use

JAMA Ophthalmol. 2014 Oct;132(10):1199-208. doi: 10.1001/jamaophthalmol.2014.1720.

Regular examinations for toxic maculopathy in long-term chloroquine or hydroxychloroquine users.

Nika M[1], Blachley TS[1], Edwards P[2], Lee PP[1], Stein JD[1]

- Among all pts on paquenil
  - ≈50% had regular eye exams
  - ≈20% had diagnostic testing as recommended per AAO Guidelines
- Among high risk patients
  - 27% had no exam within last 5 years
  - 34% had no diagnostic testing in last 5 years
- Patients seen by rheumatologist had 77.4% increased likelihood or regular eye care

Spectral Domain: Many Options

- Ease of use
- Customer support
- Integration of other technology
  - FAF
  - Color
  - MSI
- Reputation of company

What's new in OCT?

- MORE SCANS PER SECOND
  - Up to 70 k
- WIDEFIELD
- COMBO INTRUMENTS
  - PHOTOS
  - FAF
  - ANTERIOR SEG
- ANGIOGRAPHY

Fundus Autofluorescence (FAF) Imaging

- Non-invasive technique which utilizes fluorescent properties of lipofuscin to study the health and viability of RPE/ photoreceptor complex

Fundus Autofluorescence (FAF) Imaging

- In AMD, may help differentiate from similar entities
- FAF variation may precede retinal changes, and may be prognostic for those patients that will continue to develop vision loss

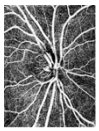
OCT Angiography: the Next Chapter in Posterior Imaging

Images retinal microvasculature without dye injection

Displays structure and function from a single imaging system

2002: Time Domain OCT

2006: Spectral Domain OCT

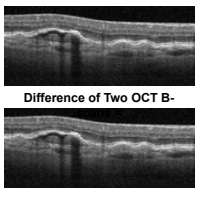


2014: OCTA

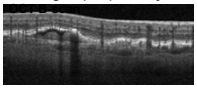
Principles of AngioVue OCTA

OCTA uses motion contrast to detect flow from OCT data

- Rapidly acquires multiple cross-sectional images from a single location on the retina
- Flow is the difference in signal between two sequential B-scans



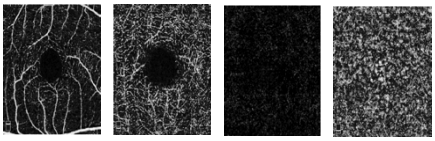
Difference of Two OCT B-



Flow Signal (Red) Overlay on

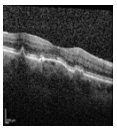
Vascular Imaging…No Referral Needed

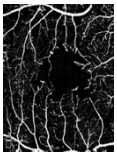
- See retinal vasculature without referring patients out of the practice
- Visualize signs of disease earlier and make more intelligent referrals
- Manage more pathology to keep patients in the practice longer
- Elevate the practice with state-of-the-art imaging technology

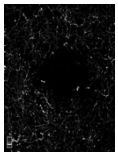


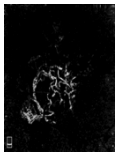
The Utility: Applications of OCTA in the Primary Eye Care Practice

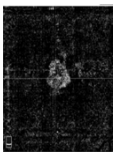
- Observing dry AMD for conversion to wet
- Monitoring diabetic patients
- Visualizing vascularization in PEDs
- Identifying CNV in central serous
- Examining glaucoma patients for vascular changes











Superficial & Deep Plexus in Diabetic Retinopathy

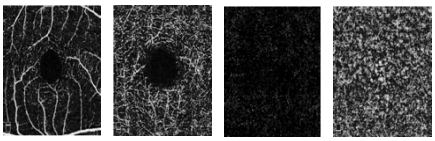
Outer Retinal Zone in Neovascular

Outer Retinal Zone in PED Case

Images courtesy of Richard Rosen, MD, Pravin Dugel, MD & Alan Franklin, MD, PhD

A New Approach to Visualizing Blood Flow

- Patient Benefits
  - Reduces patient burden to allow more frequent imaging
  - Avoid potential side-effects of fluorescein injection
- Clinical Benefits
  - Faster than a dye-based procedure
  - Ultra-high resolution imaging of retinal microvasculature
  - 3D visualization: segments retinal vasculature into individual layers



Comparison of Vascular Imaging Modalities

	FA	ICG	OCTA
Test Administration	Dye Injection Series of Photos	Dye Injection Series of Photos	Non-Invasive, Dye-Free, OCT Scan
Image Presentation	2-Dimensional	2-Dimensional	3-Dimensional, Individual Layers of Vasculature, Allows Localization of Abnormal Flow
Vasculature Imaged	Retinal Vessels	Choroidal Vessels	Retinal and Choroidal Vessels
Blood Flow Visualization	Dynamic, Leakage and Pooling Visible	Dynamic, Leakage and Pooling Visible	Static, Shows Flow Information at a Fixed Point in Time
Field of View	30° - 150°	30° - 150°	?
Procedure Time	30 Minutes	30 Minutes	30 Seconds

Macular Hole

- Present as a circular to oval depression of varying degrees in the avascular area of the macula
  - May have surrounding cuff of edema
- Most common cause is idiopathic
  - other causes include blunt trauma, severe myopia, solar retinopathy, CME
- Highest incidence in 7th decade of life
- Women 2x as often as men

Macular Hole

- Vision typically 20/80 to 20/200 with full-thickness hole
- 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
- Watzke-Allen sign useful to differentiate true hole from similar appearance
- OCT very useful

Classic Hole Classification

- Stage I: Foveal detachment, aka Impending hole
- Stage II: Partial thickness holes
- Stage III: Full thickness hole
- Stage IV: full thickness hole with vitreous separation

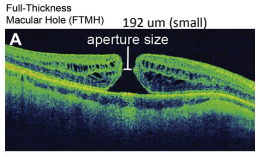
New IVTS Classification

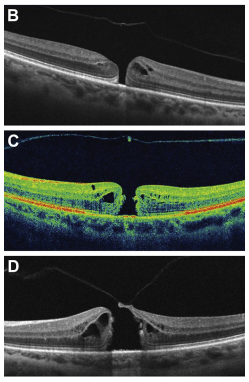
- VMA:Vitreo-Macular Adhesion (stage 0)
- VMT: Vitreo-Macular Traction (stage 1)
- LMH: Lamellar Macula Hole (Stage 2)
- FTMH: Full Thickness Macula Hole (Stage 3,4)
- Macular pseudohole

FTMH

- Definition: Full thickness macular hole that affects all macular layers from ILM to RPE
- Size
  - Small: ≤250 um
  - Medium: 250um to 400um
  - Large ≥ 400 um
- Presence or absence of VMT
- By cause
  - Primary: Initiated by VMT (formerly idiopathic)
  - Secondary: from associated disease or trauma

FTMH





FTMH

- Small holes
  - Small rate of spontaneous closure
  - Very high surgical closure rate (almost 100%)
  - Best response to pharmacologic vitreolysis
- Medium holes
  - High surgical closure rate (>90%)
  - Decent response to pharmacologic vitreolysis
- Large holes
  - High surgical closure rate (75-90%)
  - No response to pharmacologic vitreolysis
  - ½ of all holes are large at time of diagnosis

LMH

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

Macular Pseudohole

- Definition:
  - Invagination or heaped foveal edges
  - Concomitant ERM with central opening
  - Steep macular contour to the central fovea with near-normal central foveal thickness
  - **No loss of retinal tissue**

Pseudohole

- Conservative management
- PPV with membrane peel if decreased VA
- Monitor
- HAG

VMT: Vitreomacular Traction

- VMT syndrome is characterized by a partial detachment of the posterior detachment with persistent adherence to the macula
  - Can lead to CME, ERM, and macular hole formation
- Once thought to be relatively rare, with advent of OCT now being seen more and more
  - In one study, 8% of pts were thought to have VMT by clinical observation only, but 30% by OCT

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

VMT

- More commonly encountered in older women
  - Can occur in either sex, and age, no apparent racial predilection
- Aphakia and pseudophakia are protective, as these patient typically have a complete PVD
- Pts may report decreased vision, metamorphopsia and photopsia

VMA vs. VMT: Duker

VMA

- Evidence of vitreous cortex detachment from retinal service
- Attachment of vitreous within 3 mm of fovea
- **No detectable change in foveal contour or underlying tissues**
- Focal: <1500 um
- Broad: >1500 um

VMT

- Evidence of vitreous cortex detachment from retinal service
- Attachment of vitreous within 3 mm of fovea
- **Distortion of foveal surface, intraretinal structural changes, and/or elevation of fovea, but no full thickness interruption of retinal layers**

VMT

- Clinically, very hard to diagnose
  - PVD with adherence to macular area
  - Can present as macular surface wrinkling/ striae , similar to ERM, or loss of foveal reflex
  - May also note a thickened posterior hyaloid membrane
  - Retinal blood vessel distortion straightening may be present
  - Retinal thickening /macular edema may be associated

–OCT IS THE KEY!!!!

VMT

- Natural progression of disease is rather variable
  - Slow progression possible with near normal acuity
  - Approx 10% will have spontaneous PVD and resolution
- Therefore, close monitoring my be advised for some patients

VMT

- In patients with poor vision, or symptomatic, a pars planar vitrectomy (PPV) may be considered
  - Duration, severity should also be considered
- Literature repots up to a 75% success rate and improvement of vision following PPV

Jetrea™ (ocriplasmin)

- New(ish) treatment for VMT
- recombinant form of human plasmin that dissolves the protein links that form between the vitreous and macula, separating them non-surgically
- FDA approved late 2012, available in US January 14, 2013

Jetrea™ (ocriplasmin)

- 652 eyes, 64 with ocriplasmin, 188 with placebo. Single 125 ug injection
- At 28 days
  - VMA resolved 26.5 %vs 10.1%
  - Total PVD in 13.4 %vs 3.7%
  - Nonsurgical closure of macular holes: 40.6% vs 10.6%
  - VA improved three lines or more: 12.3 vs 6.4%
- At 6 mos, 17.7% of pts vs. 26.6% underwent vitrectomy

Jetrea™ (ocriplasmin)

- Adverse events: 68.4% vs. 53.3%
  - Floaters (16.85 vs. 7.7%) eye pain, photopsia , sub-conjunctival hemorrhage
  - Serious events were 7.7% vs.10.7%
- COST:

  –$3950!!!

Expansile Gas injection

- 15 eyes, 14 pts with symptomatic VMT injected intravitreally with 0.3ml perfluoropropane (C_3F_8), expansile gas
  - At 1 mos, traction release in 40% of pts (6/14)
  - At 6 mos, traction release in 60% (9/14)
  - Foveal contour restored in 47% of eyes
  - No gain in VA
  - Only 33% of pts had to have PPV
  - Horiz diameter < 750um, foveal thickness < 500 um, and low vitreous face reflectivity were very responsive (100%)

Epi-retinal Membrane

- AKA macular pucker, cellophane maculopathy
- Can be secondary to peripheral retinal disease, such as detachment or tear; a retinal vascular disease such as BRVO; inflammation; trauma or idiopathic
- Idiopathic tend to be more mild and non-progressive vs. those after retinal tear

Epi-retinal Membrane

- VA can range from 20/20 to 20/200 or worse
  - Studies show > 5% have worse than 20/200
- Often metamorphopsia is only complaint with idiopathic ERM
- Fewer than 20% of cases are bilateral
- Surgical removal is considered if severe vision loss or distortion

ERM

AGE	INCIDENCE
< 60	1.7%
60-69	7.2%
70-79	11.6%
80+	9.3%

BLUE MOUNTAIN EYE STUDY, AUSTRALIA

Epi-retinal Membrane

- Consider surgery if:
  - VA 20/40 or worse
  - Symptomatic
  - Visual need of patient
- 30 minute procedure
- Make sure you have an experienced surgeon!!

Central Serous Retinopathy

- Common disorder of unknown etiology which typically affects men between age 20 and 45
  - Males to females 10:1
- Serous detachment of neurosensory retina due to leakage from small defect in RPE

Central Serous Retinopathy

- Pt typically presents with fairly recent onset of blurred VA in one eye with a scotoma, micropsia, or metamorphopsia
  - VA typically 20/30-20/70
  - Often correctable with low hyperopic RX
  - Unilateral in 70% of cases

Central Serous Retinopathy

- Appears as a shallow round or oval elevation of the sensory retina often outlined by a glistening reflex
- FA is helpful in providing definitive diagnosis
  - Classic Smoke stack appearance (occasionally)
  - Ink-blot appearance
- OCT shows marked elevation

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?

Central Serous Retinopathy

- 80-90% of pts will undergo spontaneous resolution and return to normal (or near normal) VA within 1-6 mos.
  - >60% resolve back to 20/20
  - Rare to have vision remain < 20/40
- Approx 40% will get recurrence
- CNVM is VERY rare occurrence, but possible

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

Treatment

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

Solar Maculopathy

- Damage to the outer layers retina as shown on OCT
  - Outer segment of photoreceptors and RPE
- Clinical exam, small yellowish lesion
- Acuity typically 20/40-20/60
  - Little to no correlation with appearance and acuity
- Greater risk in younger individuals who are more likely to start at sun or eclipse
  - With clear lenses
  - Also, schizophrenic pts, pts on LSD, etc.

Macular Schisis

- Relatively new entity, ≈1999 by Takano and Kishi
  - Prior to this, misinterpreted as shallow RD or even edema
- With OCT, thought to be not uncommon in highly myopic individuals with posterior staphyloma
- Characterized by intraretinal splitting, in both inner and outer retina, with cystoid spaces

Macular Schisis

- Fairly stable with time, with mild fluctuations in vision
- Treatment (vitrectomy) generally only recommended if vitreal traction, as may lead to macula hole
- Consider OCT in high myopes with central vision problems

OCT: Final Thoughts

- Has ushered in a whole new understanding of retinal disease
- Fast becoming the standard of care
- Many models /makes available

- THANK YOU!!