RETINA 2018

KELLY MITCHELL

OBJECTIVES

HIGHLIGHT NEW DIAGNOSTIC & TREATMENT OPTIONS

REVIEW DIAGNOSTIC KEYS OF SELECT RETINAL DISEASES

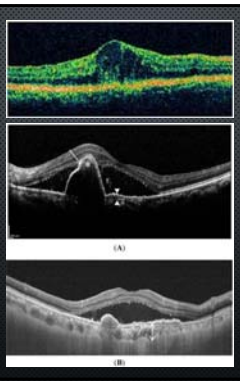
DISCUSS USE OF IMAGING AND REFERRAL RECOURSES FOR PATIENT BENEFIT

OCT

VERY USEFUL INFORMATION

SAFE AND FRIENDLY

OCT



Time Domain TD

Spectral Domain SD

Swept Source SS

ssOCT

Color	Wavelength
violet	380–450 nm
blue	450–495 nm
green	495–570 nm
yellow	570–590 nm
orange	590–620 nm
red	620–750 nm

NO MOVING REFERENCE ARM

1065 NM (INFRARED) LASER

SWEPT THROUGH DIFFERENT FREQUENCIES

FASTER IMAGE COLLECTING SYSTEM

100,000 A SCANS/IMAGE

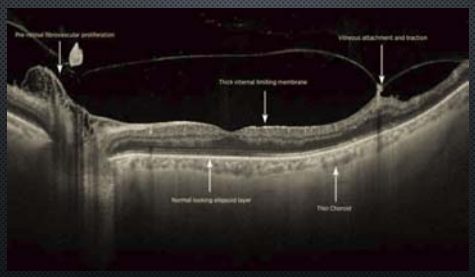
ssOCT

SAME OR BETTER RESOLUTION

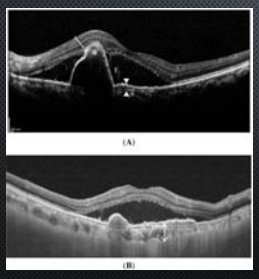
LONGER RASTERS/BIGGER CUBES

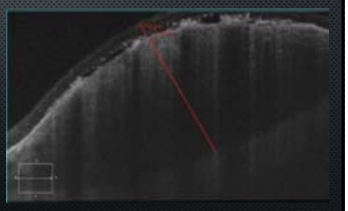
IMAGES OF DEEPER STRUCTURES

SSOCT: LONGER RASTERS/BIGGER CUBES



SSOCT: IMAGES OF DEEPER STRUCTURES





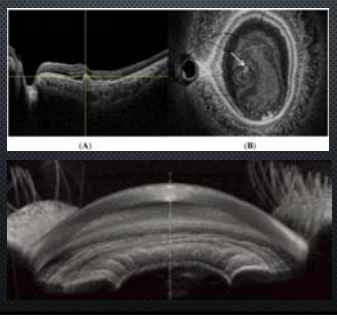
SSOCT

IMAGES THROUGH MEDIA OPACITIES

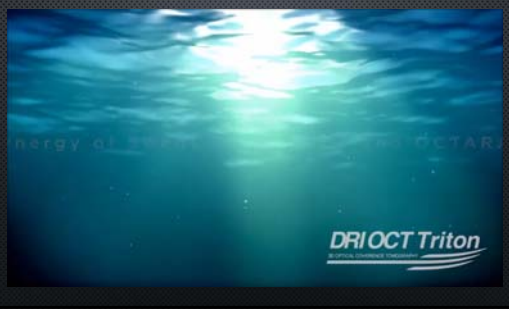
IMPROVED PATIENT COMFORT

ENFACE IMAGING

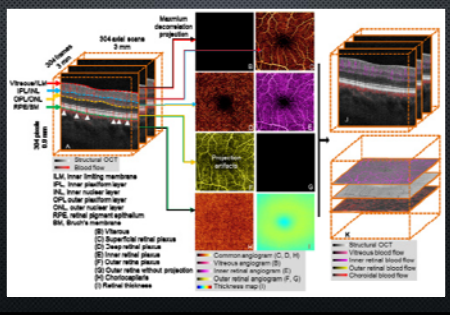
SSOCT: ENFACE



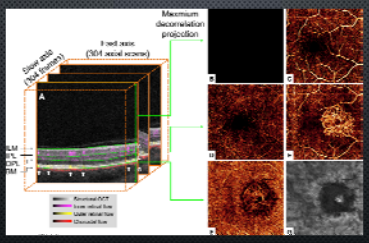
OCT ANGIOGRAPHY



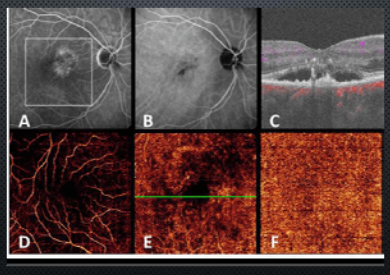
OCT ANGIOGRAPHY



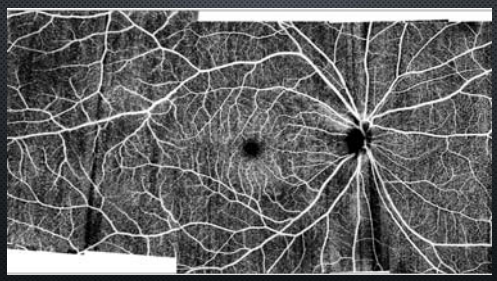
OCT ANGIOGRAPHY



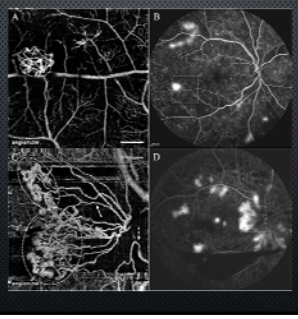
OCT ANGIOGRAPHY



OCT ANGIOGRAPHY



OCT ANGIOGRAPHY



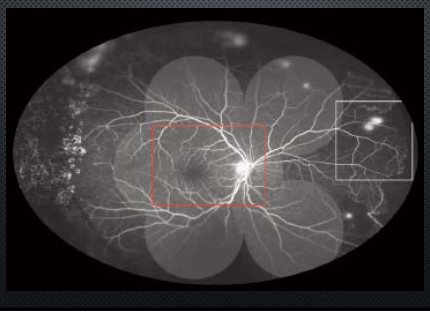
SSOCT: WHAT WE KNOW

- SSOCT IS NOW AVAILABLE AND MAKING A POSITIVE CLINICAL IMPACT
- SSOCT IMAGING: DEEPER STRUCTURES, POSTERIOR POLE & OPTIC NERVE
- OCT ANGIO WILL GROW IN CLINICAL UTILITY

SSOCT: WHAT WE DO NOT KNOW (YET) ?

- IMAGING THROUGH MEDIA OPACITIES MATTER?
- BETTER PATIENT COMFORT REAL OR MYTH?
- HIGHER PRICE OF THE MACHINE WORTH IT?

FLUORESCEIN ANGIOGRAPHY (FA)



PRACTICAL ASPECTS OF FA

Injection into arm or hand vein

Transit Phase (10 to 15 seconds from injection time)

- Initial filling of retina and Choroidal vessels
- Choroidal vessels fill in a patchy lobular pattern
- Retinal vessels have a longer course to fill slightly after the choroidal vessels

Arteriovenous phase = period of filling of arteries & capillaries & ends with laminar filling of veins. Occurs at one minute after injection

Recirculation phase = Over next few minutes (4-8) dye recirculates with decline of fluorescence.

SAFETY ISSUES OF FA

100% yellowing skin/conjunctiva for 6-12 hours and yellow-orange change of urine for 24-36 hours.

10% Nausea and vomiting or vasovagal

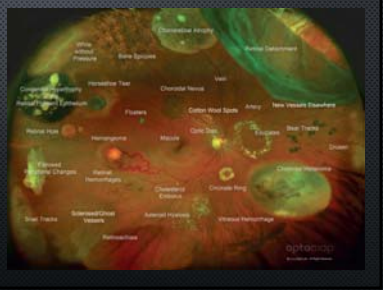
Extravasation during injection is not uncommon (treat with ice), but severe reaction: granuloma, toxic neuritis or local tissue necrosis are rare.

1% Urticarial (anaphylactoid) reaction

0.001-2% Anaphylactic reaction (cardiovascular shock)

Many Avoid FA in first trimester although no clear teratogenic effects have been linked.

WIDE FIELD IMAGING



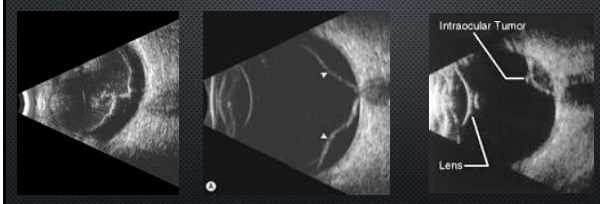
ULTRASOUND BASICS

When?
Media
Measurement

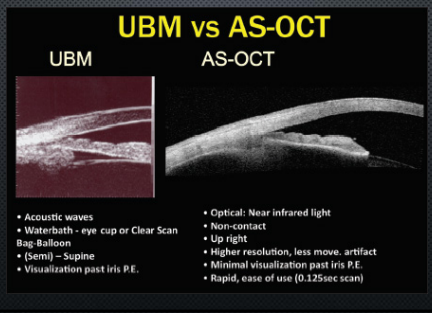
B-Scan

Frequency	Depth	Field
Low Frequency 1-5 MHz	Orbital Tissues/ Abdominal	High
Medium Frequency 7-10 MHz (B Scan)	Retina, Vitreous, Optic Nerve (940μ)	40 mm
High Frequency 30-50 MHz (UBM)	Ant Chamber, Angle (40μ)	5-10 mm

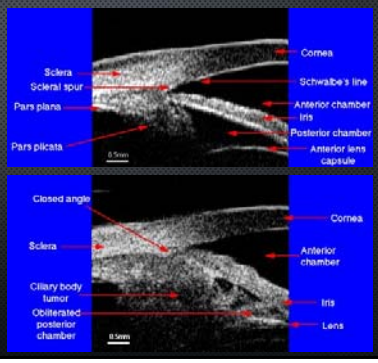
ULTRASOUND BASICS



UBM VS ASOCT



UBM USE



FUNDUS AUTOFLUORESCENCE (FAF)

USEFUL INFORMATION

SAFE AND "FRIENDLY"

FAF

- Lipofuscin (LF) is a marker for aging RPE cells
- Dependent on outer segment renewal
- Balance of RPE accumulation and clearance

FAF

Color	Wavelength
violet	380–450 nm
blue	450–495 nm
green	495–570 nm
yellow	570–590 nm
orange	590–620 nm
red	620–750 nm

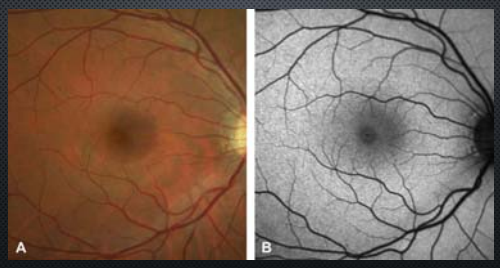
- RPE LF has different fluorophores with discrete spectra
- LF has broad excitation spectrum 300-600nm
- LF has broad emission spectrum 480-800nm

FAF

Normal FAF topographic distribution

- **No FAF** (Normal Dark Areas)
  - Optic Nerve Head and Retinal Vessels
  - Fovea: luteal pigments absorb blue light by
- **Intermediate level FAF**
  - Parafoveal area
- **Diffuse Background FAF**
  - Peripheral posterior pole and beyond

FAF



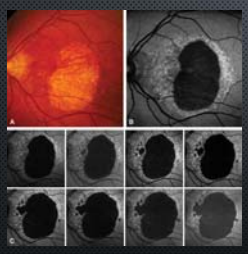
REDUCED FAF SIGNAL

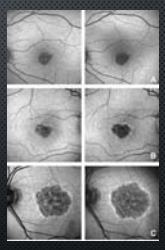
- REDUCTION OF RPE LF DENSITY
  - RPE LOSS OR ATROPHY
- ABSORPTION OF EXCITATION OR EMISSION SPECTRUM
  - ABNORMAL PIGMENT, FLUID OR DEPOSIT

INCREASED FAF SIGNAL

- RPE LF ACCUMULATION
  - EXCESS LF IN SICK RPE
- LF CONTAINING PIGMENT, FLUID OR DEPOSITS

ABNORMAL FAF SIGNAL





HYDROXYCHLOROQUINE

SCREENING RECOMMENDATIONS

AN IMAGING PLAN

SCREENING RECOMMENDATIONS

THE RISK OF TOXICITY OF HCQ/CQ IS HIGHER THAN PREVIOUSLY THOUGHT

THE SENSITIVITY OF NEW DIAGNOSTIC TECHNIQUES: SD-OCT, FAF AND MFERG

TOXICITY OF HCQ/CQ

- Chloroquine (CQ) & Hydroxychloroquine (HCQ) mechanism of toxicity is still unclear
- Have short term effects on photoreceptors
- Bind to melanin and RPE cells
- Binding to melanin may serve to remove these toxins from sites of damage
- Macular location
- Light absorption or cone metabolism may play a role

RISK OF TOXICITY OF HCQ/CQ

- Old prevalence data unclear (0.08 -- 0.05%)
- New prevalence data is higher 0.68%
- Dependent on duration of use (cumulative dose)
- Years 1-5 prevalence was lower 0.2%
- Years 5-7 prevalence increased to nearly 1%

RISK OF TOXICITY OF HCQ/CQ

- Years 5-7 prevalence increased to nearly 1%
- Maybe even greater with continued use
- The new screening recommendations supports screening as the risk of toxicity approaches 1%
- Reason for annual screening after 5 years of use

CLINICAL PICTURE OF TOXICITY

BILATERAL BULL'S-EYE MACULOPATHY

- RING OF RPE DEPIGMENTATION THAT SPARES A FOVEAL ISLAND
- PARACENTRAL SCOTOMAS MAY PRODUCE READING DIFFICULTIES **BEFORE**
  - VISUAL ACUITY LOSS
  - RPE CHANGES

CLINICAL PICTURE OF TOXICITY

BILATERAL BULL'S-EYE MACULOPATHY

- WITH CONTINUED DRUG EXPOSURE THE RPE ATROPHY WILL SPREAD INTO THE FOVEA
- LOSS OF VISUAL ACUITY
- SEVERE CASES SHOW WIDESPREAD RPE & RETINAL ATROPHY
- SEVERE LOSS OF ACUITY, PERIPHERAL VISION AND NIGHT VISION

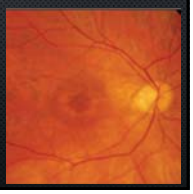
CLINICAL PICTURE OF TOXICITY

Bull's-eye maculopathy

- Do not show much clinical recovery
- May see continued depigmentation & functional loss for 1 year or more after drug is stopped

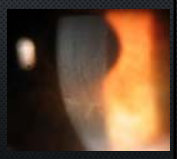
Reason for late progression

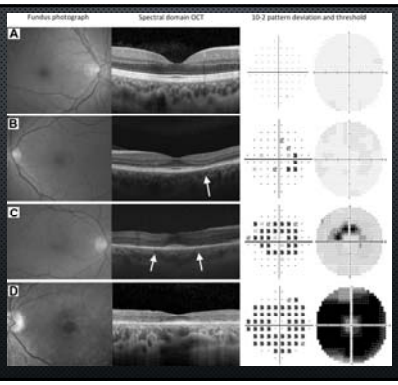
- Gradual loss of cells injured by drug
- Reservoir of drug causes more damage
- Clearance of drug can take months



CLINICAL PICTURE OF TOXICITY

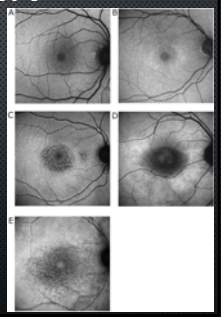
Cornea verticilata
Whorl-like intraepithelial deposits
HCQ less so than CQ
Suggest drug retention
Not a marker for retinal damage





FAF PICTURE OF TOXICITY

1. Pericentral ring of increased FAF
2. Pericentral mottled loss of FAF with increased FAF in adjacent peripheral area
3. Pericentral ring with total loss of FAF with increased FAF in adjacent peripheral area
4. Mottled loss of FAF in the posterior pole and increased FAF in adjacent peripheral retina



SDOCT PICTURE OF TOXICITY

1. "Moth-eaten" photoreceptor inner segment/outer segment
2. Loss of parafoveal photoreceptor IS/OS
3. Thinning of parafoveal outer nuclear layer
   - Parafoveal collapse (toward RPE) of overlying inner retinal layers "sink hole effect"
   - Loss of foveal depression
4. Preservation of subfoveal photoreceptor IS/OS

"Flying Saucer" Sign
E. Chen D. Brown M. Benz R. Fish T. Wong R. Kim J. Major
Clinical Ophthalmology 2010

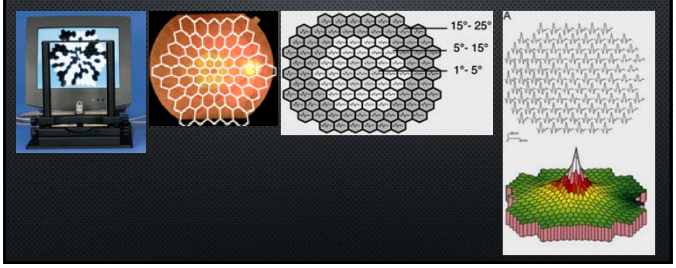
MULTIFOCAL ELECTRORETINOGRAM MFERG

Electrophysiological test of local retina function

Central 20-30 degrees tested & light adapted

Primarily Cone and bipolar cell function
Multifocal pattern gives more precise mapping
61 and 103 patterns most common (241 rarely)

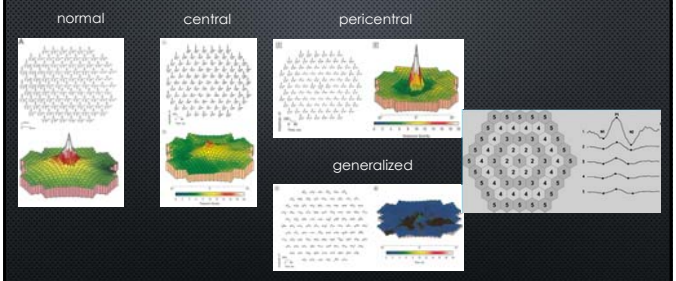
MULTIFOCAL ELECTRORETINOGRAM MFERG



MFERG PICTURE OF TOXICITY

1. Pericentral waveform loss
2. Central waveform loss
3. Generalize depression
4. Peripheral waveform loss
5. Ring Ratio Abnormalities
   Increased R_1/R_2,

MFERG PICTURE OF TOXICITY



CLINICAL ASSESSMENT TOOLS

COMPLETE EYE EXAMINATION

MACULA ASSESSED FOR ANY CHANGES DUE TO UNRELATED RETINAL DISEASE THAT COULD BE CONFUSED WITH HCQ/CQ (BULLS-EYE) RETINOPATHY

CONSIDERED A DOCUMENTATION TOOL NOT A SCREENING TOOL FOR HCQ/CQ TOXICITY

CLINICAL ASSESSMENT TOOLS

AUTOMATED WHITE THRESHOLD VISUAL FIELDS (10-2 WHITES 30-2 ASIANS)

- RESPECT NONSPECIFIC VF LOSS, PROMPTLY REPEAT WHEN NEW CHANGES APPEAR OR IF TEST QUALITY IS POOR
- DEPRESSED CENTRAL OR PARAFOVEAL AREA COULD INDICATE EARLY TOXICITY AND INDICATES THE NEED FOR FURTHER TESTING:
- ADVANCED TOXICITY WILL TYPICALLY SHOW A WELL DEVELOPED PARACENTRAL SCOTOMA

THE GOAL OF THE SCREENING IS TO IDENTIFY THE TOXICITY BEFORE VISION LOSS OCCURS

CLINICAL ASSESSMENT TOOLS

SDOCT, MFERG, FAF CAN OBJECTIVELY DOCUMENT DAMAGE DUE TO HCQ OR CQ

THE STUDIES COMPARING THESE TO VF ARE FEW

THE OPTIMAL TEST COMBINATION CURRENTLY RECOMMENDED:

- PRIMARY VF AND SDOCT
- SECONDARY (AS NEEDED) MFERG & FAF

AAO 2016 RECOMMENDATIONS 1

BACKGROUND

AAO SCREENING RECOMMEDATIONS FOR CHLOROQUINE (CQ) AND HYDROXYCHLOROQUINE (HCQ) RETINOPATHY ARE REVISED IN LIGHT OF NEW INFORMATION ABOUT THE PREVALENCE OF TOXICITY, RISK FACTORS, FUNDUS DISTRIBUTION, AND EFFECTIVENESS OF SCREENING TOOLS.

PATTERN OF RETINOPATHY

THE LOCUS OF TOXIC DAMAGE IS PARAFOVEAL IN MANY EYES, ASIAN PATIENTS OFTEN SHOW AN EXTRAMACULAR PATTERN OF DAMAGE.

DOSE

A MAXIMUM DAILY HCQ USE OF ≤5.0 MG/KG REAL WEIGHT, WHICH CORRELATES BETTER WITH RISK THAN IDEAL WEIGHT. THERE ARE NO SIMILAR DEMOGRAPHIC DATA FOR CQ, BUT DOSE COMPARISONS IN OLDER LITERATURE SUGGEST USING ≤2.3 MG/KG REAL WEIGHT.

AAO 2016 RECOMMENDATIONS 2

Risk of Toxicity

Toxicity is dependent on daily dose and duration of use. At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years. However, even after 20 years, a patient without toxicity has only a 4% risk of converting in the subsequent year.

Major Risk Factors

High dose and long duration of use are the most significant risks. Other major factors are concomitant renal disease, or use of tamoxifen.

Screening Schedule

A baseline fundus examination should be performed to rule out preexisting maculopathy. Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.

AAO 2016 RECOMMENDATIONS 3

Screening Tests

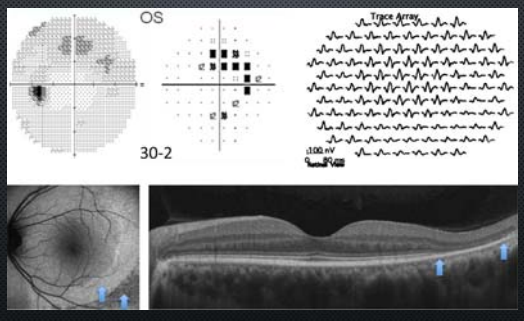
The primary tests: **10-2/30-2 VFs and SD OCT**. These should look beyond the central macula in Asian patients. **mfERG** can provide objective corroboration for visual fields, and **FAF** can show damage topographically.

Toxicity

Retinopathy is not reversible, and there is no present therapy. Recognition at an early stage (before it is visible in the fundus) is important to prevent central visual loss. However, questionable test results should be repeated or validated with additional procedures to avoid unnecessary cessation of drug.

Counseling

Patients and prescribing physicians should be informed about risk of toxicity, proper dose levels, and the importance of regular annual screening.



AMD

- Stop smoking
- Vitamins: AREDS 2
- Drugs over laser
- Bevacizumab, Ranibizumab, Aflibercept
- Surgery:
- Retinal Translocation, IMT, Stem cells
- RPE 65 gene (Luxturna) eye injection therapy for Mutations in that gene are responsible for early onset blindness from Leber congenital amaurosis, some forms of RP

DIABETIC RETINOPATHY

- Prevention: ABCs and TRACK
- Screening: yearly
- Treatment:
  - Drugs:
    - Bevacizumab, Ranibizumab, Aflibercept, steroid implants
  - Laser: PRP yes; Focals much less
  - Surgery: smaller gauge

VITREOUS

- VMT: Ocriplasmin
  - RCT: yes 40% success rate (community: 25-30%)
    - phakic, 1DD or less no ERM do better
  - concerns: 5% have odd vision loss and cost ($$$)
- Floaters: vitrectomy, YAG, drugs
  - RCT: no, but many surgeons offer it

ANY QUESTIONS……