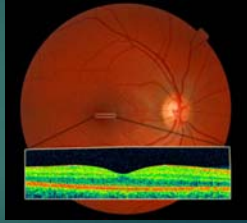


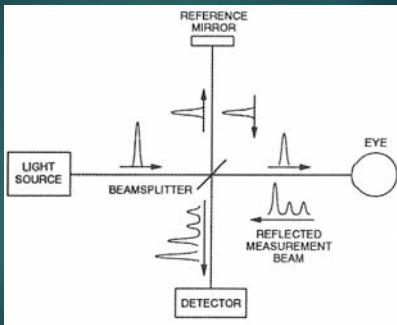
### OCT 101

GREGORY D. SEARCY, M.D.  
ERDEY SEARCY EYE GROUP  
COLUMBUS, OHIO



### How OCT Works

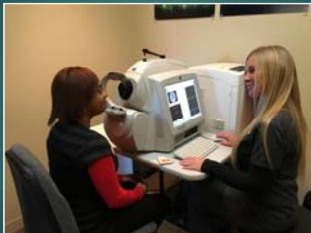
- ▶ Light beam is simultaneously sent into the eye and a reference mirror
- ▶ The light penetrates through the ocular tissue layers and is reflected back (altered)
- ▶ The returning light is compared (interferometry) to the reference light (un-altered), generating an image of the underlying tissue
- ▶ This provides cross-sectional imaging of tissue morphology in vivo



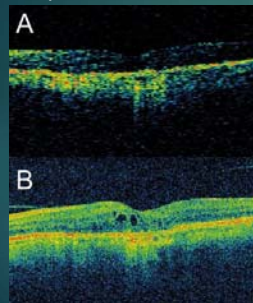
### Ocular Coherence Tomography

- ▶ Carl Zeiss Cirrus 4000
- ▶ Imaging: HD-OCT
- ▶ Methodology: Spectral Domain OCT
- ▶ Scan speed: 27,000 A-Scans per second
- ▶ A-Scan depth: 2 mm
- ▶ Axial resolution: 5  $\mu$ m
- ▶ Transverse resolution: 15  $\mu$ m
- ▶ Non-contact, high resolution tomographic and biomicroscopic imaging device

### HD Spectral Domain OCT



### HD Spectral Domain OCT

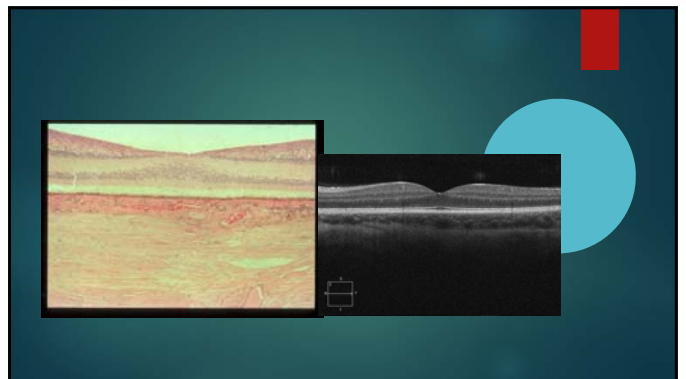
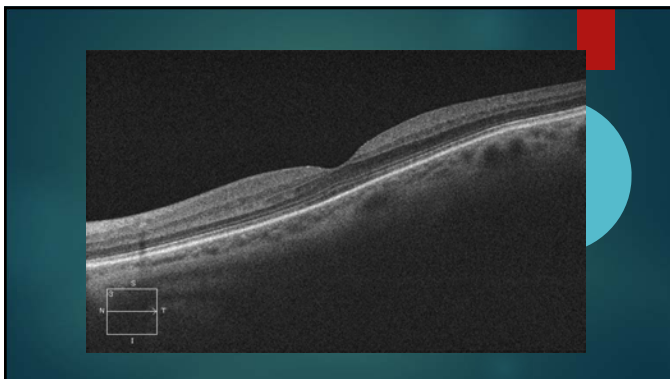
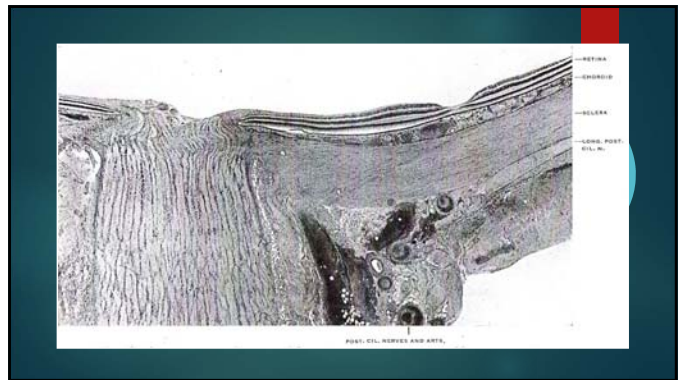
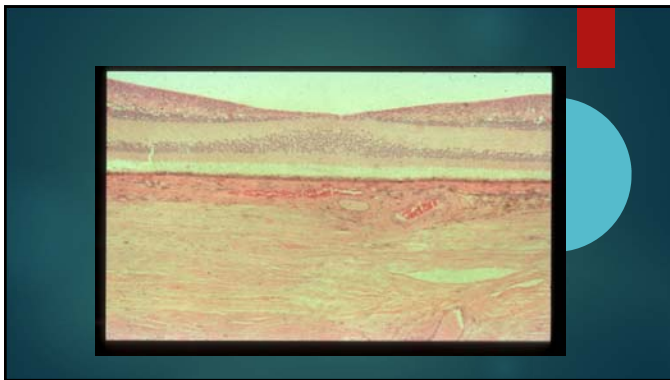


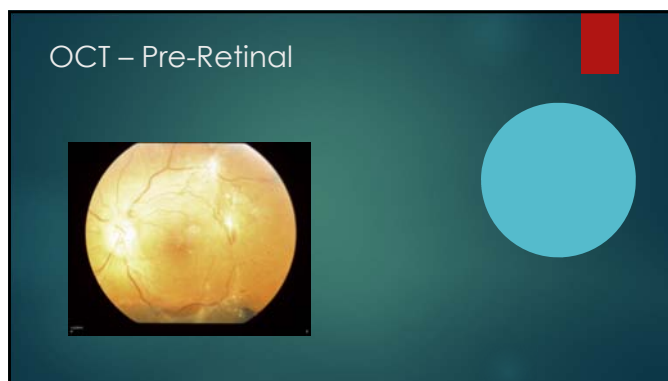
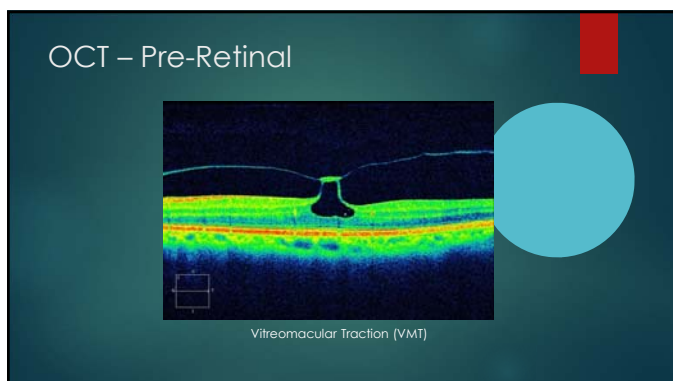
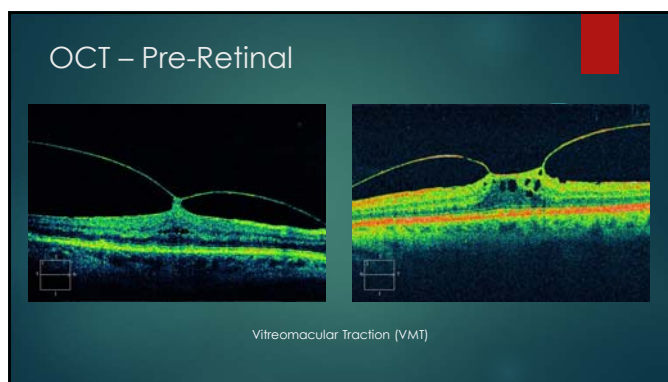
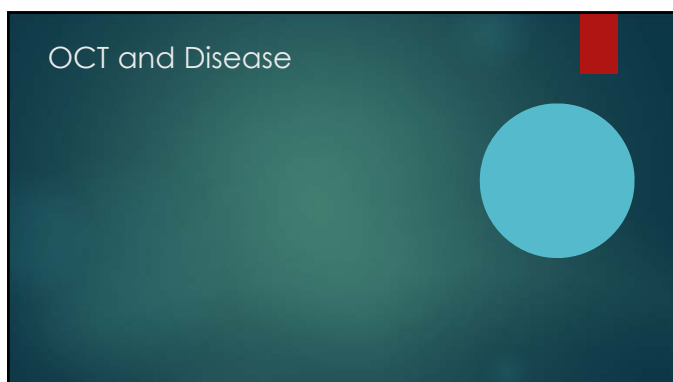
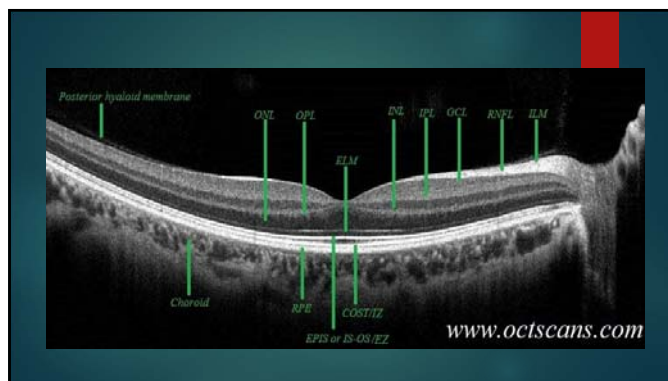
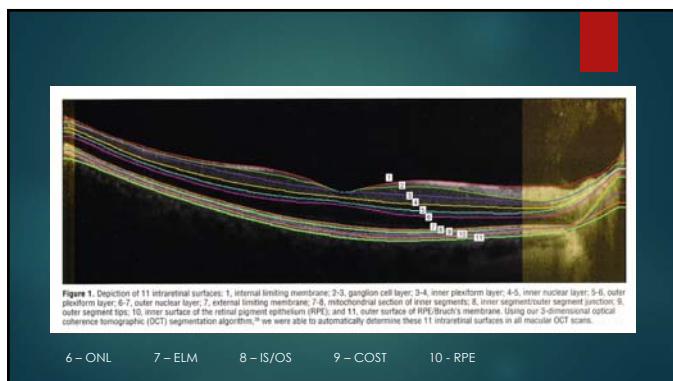
Time domain OCT (A) has been replaced by spectral domain OCT (B)  
Foveal cysts  
Barely distinguishable with the TD-OCT (A)  
Clearly identified by SD-OCT (B)

## Image Display

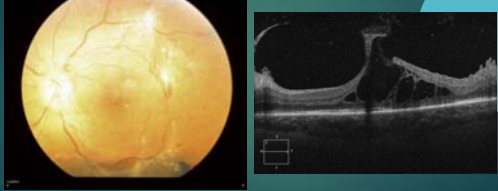
- ▶ Resolution of 5-10 micrometers in tissue
- ▶ Display is in gray scale or false color scale
  - ▶ Red-white - high reflectivity (RPE and RNFL)
  - ▶ Blue-green - low reflectivity (Ganglion cells, Photoreceptors and Choroid)
  - ▶ Black - Very low reflectivity (Vitreous)

## Normal Macula and OCT






OCT – Pre-Retinal



Diabetic Traction Retinal Detachment

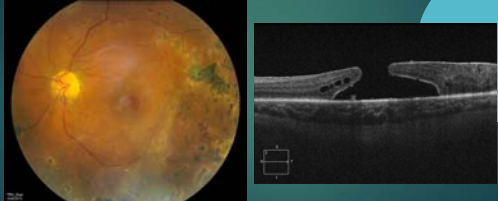
This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan displays a prominent, elevated, and irregular pre-retinal membrane, characteristic of a tractional retinal detachment. A red square is in the top right corner, and a light blue circle is partially visible on the right side.

OCT – Pre-Retinal



This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows a thin, elevated pre-retinal membrane. A red square is in the top right corner, and a light blue circle is partially visible on the right side.


OCT – Pre-Retinal



Macular Hole Following TRD Repair

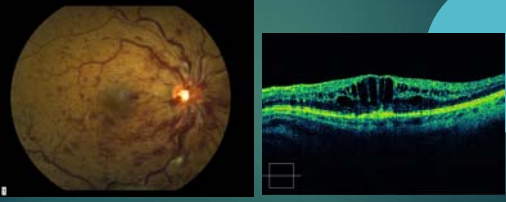
This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows a well-defined, full-thickness macular hole with a distinct gap in the retinal layers. A red square is in the top right corner, and a light blue circle is partially visible on the right side.

OCT – Intra-Retinal



This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows multiple hyporeflective cystic spaces within the retinal layers, indicating intraretinal edema. A red square is in the top right corner, and a light blue circle is partially visible on the right side.

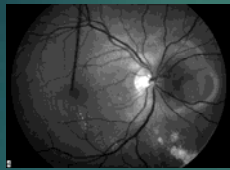
OCT – Intra-Retinal



Cystoid Macular Edema (CME) with CRVO

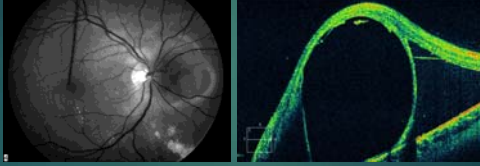
This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows multiple hyporeflective cystic spaces within the inner plexiform and outer plexiform layers, characteristic of cystoid macular edema. A red square is in the top right corner, and a light blue circle is partially visible on the right side.

OCT – Sub-Retinal




This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows a distinct layer of hyporeflective fluid located beneath the retinal pigment epithelium, indicating sub-retinal fluid. A red square is in the top right corner, and a light blue circle is partially visible on the right side.

OCT – Sub-Retinal

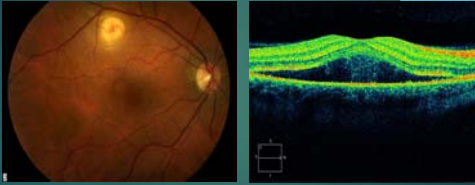


Peripapillary Capillary Hemangioma

OCT – Sub-Retinal




OCT – Sub-Retinal




Exudative Sensory Retinal Detachment from Helioid Chorioiditis

OCT – Sub-Retinal



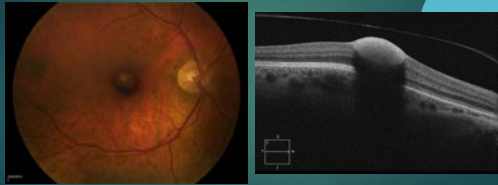
Unifocal Helioid Chorioiditis

OCT – Pre-Retinal



10/22/15

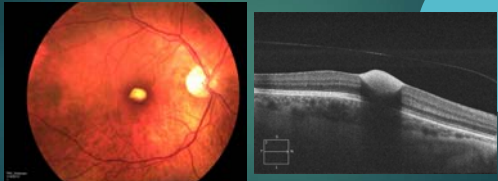
OCT – Pre-Retinal



Pre-retinal Hemorrhage from "Valsalva Retinopathy"

10/22/15

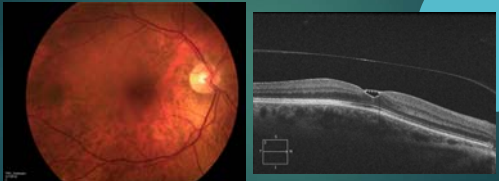
### OCT – Pre-Retinal



11/9/15 Resolving "Valsava Retinopathy"

This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan displays a prominent, dome-shaped elevation of the neurosensory retina, characteristic of a pre-retinal lesion. A red vertical bar is in the top right corner, and a light blue circle is on the right side.


### OCT – Pre-Retinal



3/7/16 Resolved "Valsava Retinopathy"

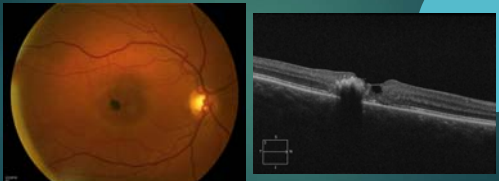
This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows a significantly flattened retina compared to the previous slide, indicating the resolution of the pre-retinal lesion. A red vertical bar is in the top right corner, and a light blue circle is on the right side.

### OCT - Intra-Retinal



This slide shows a fundus photograph of the eye. The retina appears relatively normal but with some subtle changes. A red vertical bar is in the top right corner, and a light blue circle is on the right side.


### OCT - Intra-Retinal



Intraretinal Pigment from Idiopathic Juxtafoveal Telangiectasia (IJT)

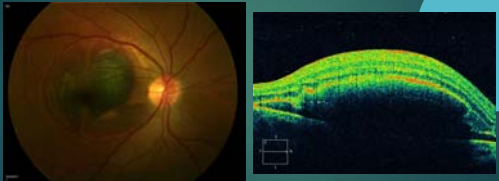
This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan highlights a localized area of hyperreflective material within the retinal layers, consistent with intraretinal pigment. A red vertical bar is in the top right corner, and a light blue circle is on the right side.

### OCT – Sub-Retinal



This slide shows a fundus photograph of the eye. The retina appears normal. A red vertical bar is in the top right corner, and a light blue circle is on the right side.

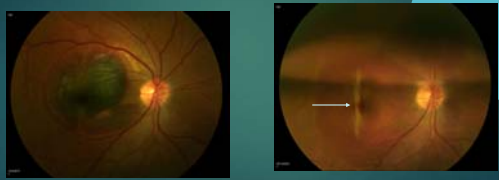
### OCT – Sub-Retinal



Subretinal Hemorrhage from a Choroidal Rupture

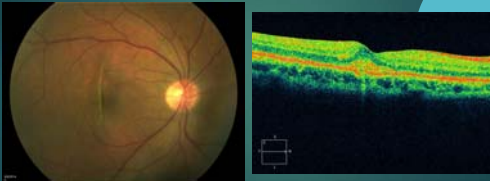
This slide shows a fundus photograph on the left and an OCT scan on the right. The OCT scan shows a distinct, dark, dome-shaped elevation beneath the retina, representing a sub-retinal hemorrhage. A red vertical bar is in the top right corner, and a light blue circle is on the right side.

### Office injection of tPA and C3F8 gas




10/4/11      10/13/11      Choroidal Rupture

### OCT – Sub-Retinal

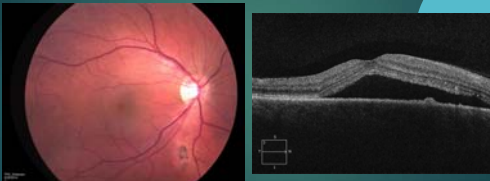


Choroidal Rupture Scar

### OCT – Sub-Retinal

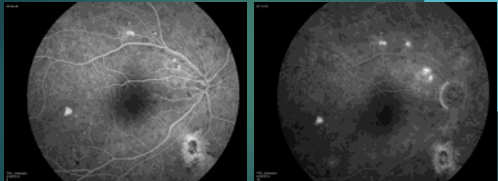


### OCT – Sub-Retinal



Exudative Retinal Detachment from Posterior Scleritis

### FA



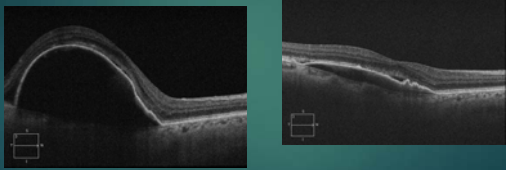
Multifocal Choroiditis and Exudative Retinal Detachment from Posterior Scleritis

### OCT – Sub-RPE



2/23/15 - 89 year old WM with 20/200 VA

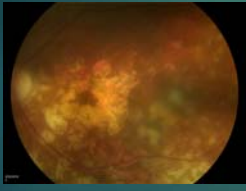
### OCT – Sub-RPE



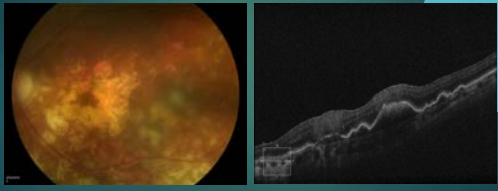
2/23/15 - 89 year old WM with 20/200 VA

3/6/15 – OCT two weeks s/p IO Avastin with VA 20/50

### OCT – Sub-RPE




### OCT – Sub-RPE



Sub-RPE Infiltrates from Primary Central Nervous System Lymphoma

### OCT – Extra-Retinal




### OCT – Extra-Retinal



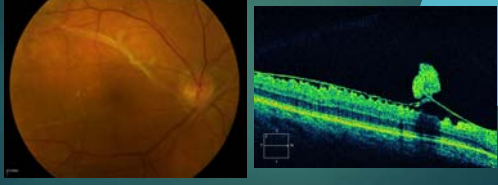
Posterior Retinal Coloboma

### OCT – Pre-Retinal





OCT – Pre-Retinal



A fundus photograph on the left shows a normal-appearing retina. To its right is an OCT scan showing a cross-section of the retina. A small, elevated, hyper-reflective lesion is visible on the surface of the retina, protruding above the normal retinal contour.

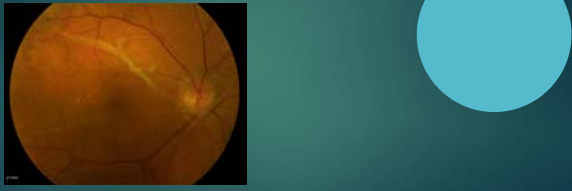
OCT – Pre-Retinal



Tree on a grassy hill?

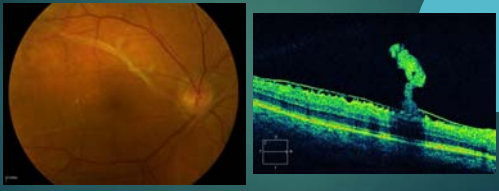
A fundus photograph on the left shows a normal-appearing retina. To its right is an OCT scan showing a cross-section of the retina. A small, elevated, hyper-reflective lesion is visible on the surface of the retina, protruding above the normal retinal contour.

OCT – Pre-Retinal



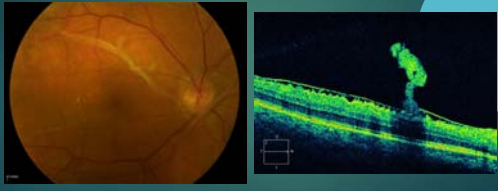
A fundus photograph on the left shows a normal-appearing retina. To its right is a large, empty light blue circle, representing the area where an OCT scan would normally be displayed.

OCT – Pre-Retinal



A fundus photograph on the left shows a normal-appearing retina. To its right is an OCT scan showing a cross-section of the retina. A small, elevated, hyper-reflective lesion is visible on the surface of the retina, protruding above the normal retinal contour.

OCT – Pre-Retinal

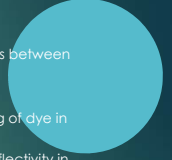


Skiing uphill?

A fundus photograph on the left shows a normal-appearing retina. To its right is an OCT scan showing a cross-section of the retina. A small, elevated, hyper-reflective lesion is visible on the surface of the retina, protruding above the normal retinal contour.


Inflammatory CME

- ▶ Cystoid macular edema
- ▶ Intraretinal edema contained in honey-comb like spaces between cells
- ▶ Abnormal perifoveal retinal capillary permeability
- ▶ FA: Multiple small focal fluorescein leaks with late pooling of dye in extracellular spaces
- ▶ OCT: diffuse retinal thickening with cystic areas of low reflectivity in inner nuclear and outer plexiform layers
- ▶ Severe cases may have subretinal fluid or optic nerve head swelling

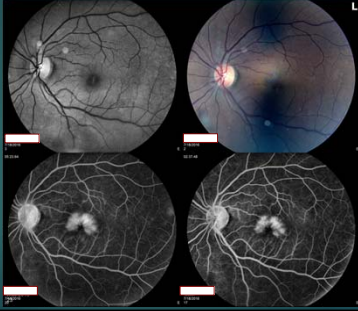



### CME

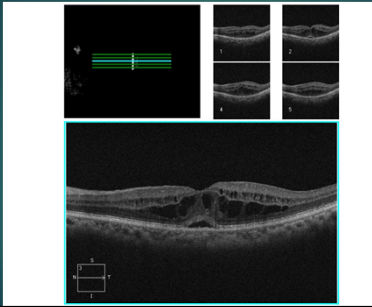
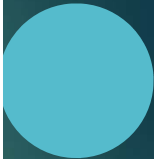
- ▶ 82 year old female 6months s/p cataract surgery
- ▶ Vision started out great then got blurred
- ▶ 20/25, 20/30, J5- OU
- ▶ IOP 27, 22
- ▶ SLE: no AC cells or flare, well-centered PCIOLs OU
- ▶ DFE: OD 0.3, trace CME, OS 0.4 CME



### CME

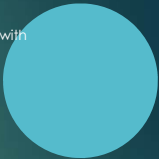



### CME

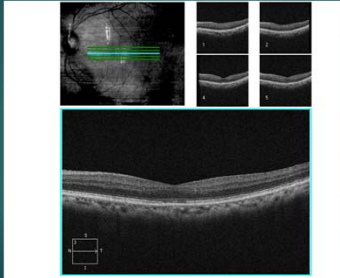




### CME

- ▶ Had been using Predforte and Bromfenac for two weeks with minimal reponse in edema.
- ▶ Subtenons kenalog 40mg in the office

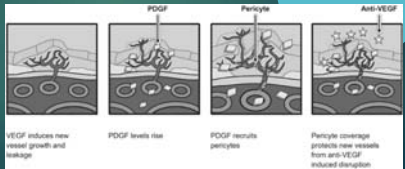
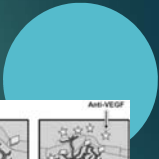


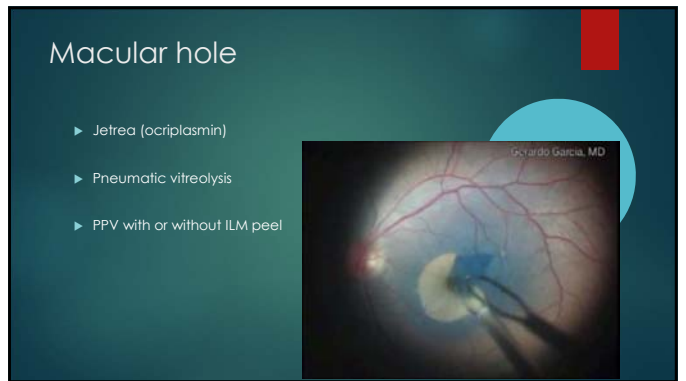
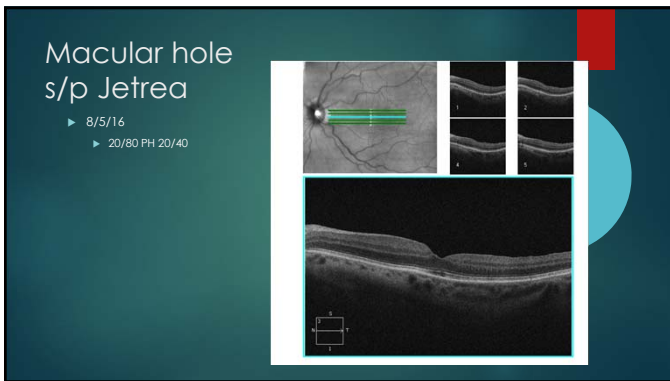
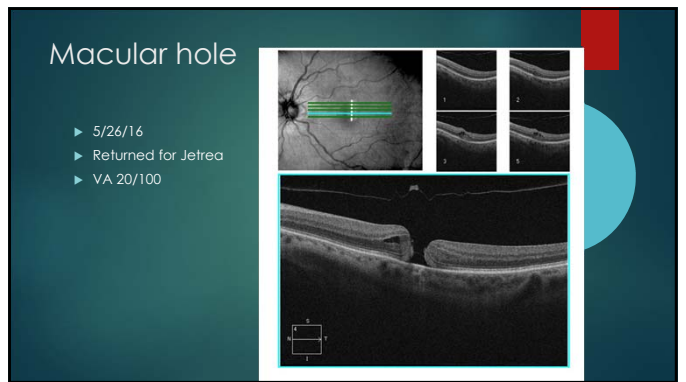
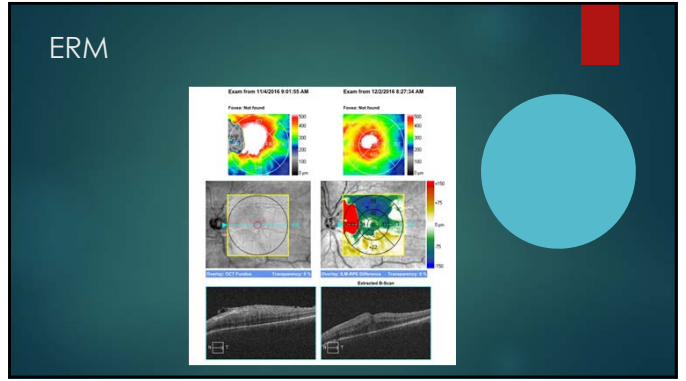
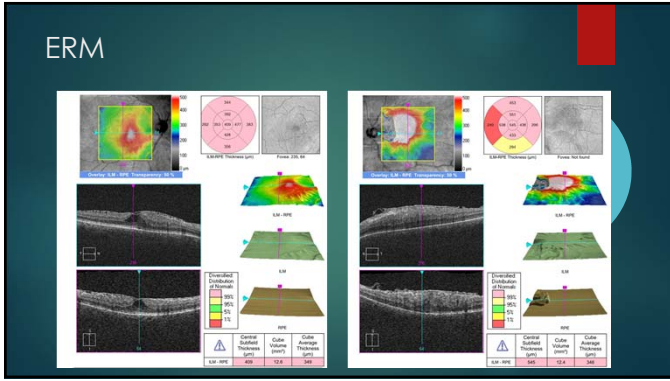
### CME (1 month later)

### Macular degeneration

- ▶ Anti-VEGF
- ▶ PDT- Visudyne
- ▶ PDGF



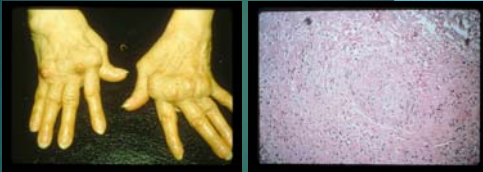
## Plaquenil Toxicity

- ▶ Hydroxychloroquine sulfate – Plaquenil (99%) and chloroquine (1%) are commonly used for rheumatologic disorders (SLE, RA, etc.) WHO Model List of Essential Medicines
- ▶ An irreversible and potentially blinding toxic retinopathy is a “rare” adverse event that may occur with long-term use in 0.1-1%
- ▶ This was based on short term studies and on end-stage observations such as visible retinal damage (bull’s eye maculopathy)

## SLE

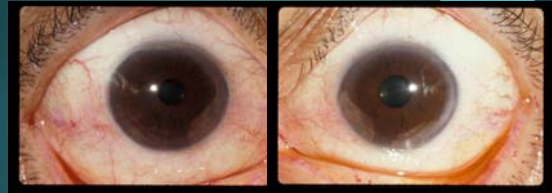


## Adult RA: Histopathology of Rheumatoid Nodule, Episcleral Nodule



- ▶ Elongated fibroblast-like cells or palisading histiocytes around a necrotic center, oriented with their long axes perpendicular to the center of the nodule, surrounded by a lymphocytic infiltrate
- ▶ Localized around a focus of microvasculitis

## Rheumatoid Arthritis Keratoconjunctivitis Sicca

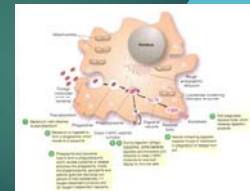


## Plaquenil – Mechanism of Action

- ▶ HCQ is a weak base that easily crosses plasma membranes
- ▶ HCQ accumulates (1000 X) in lysosomes (acidic cytoplasmic vesicles)
- ▶ HCQ increases the lysosomal pH from 4 to 6
- ▶ This pH change in turn inhibits lysosomal acidic proteases and proteolysis
- ▶ Decreased intracellular processing, glycosylation and secretion of proteins important for inflammation and immunity
- ▶ Decreased immune functions such as chemotaxis, phagocytosis and superoxide production by PMN
- ▶ Inhibits APC association of class II MHC molecules with autoantigens and therefore antigen presentation

## Ocular Immunology – Cellular Components

- ▶ Antigen Presenting Cells (APC)
  - ▶ Macrophages, Dendritic cells
  - ▶ Class I & II MHC
  - ▶ Bind
  - ▶ Phagocytize
  - ▶ Process to a peptide epitope
  - ▶ Present in Ag binding groove of MHC



## Plaquenil Toxicity

- ▶ HCQ toxicity:
  - ▶ 0.1 – 1% ¶¶¶
  - ▶ Progressive toxic effects for up to 7 years after discontinuation!
  - ▶ Little or no recovery of vision loss!
  - ▶ No treatment!



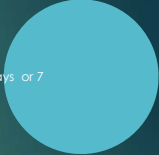
## Plaquenil Toxicity

- ▶ HCQ toxicity:
  - ▶ 0.1 – 1% ¶¶¶
  - ▶ Progressive toxic effects for up to 7 years after discontinuation!
  - ▶ Little or no recovery of vision loss!
  - ▶ No treatment!
- ▶ We now have more sensitive methods to detect early toxicity with SD-OCT, mERG, 10-2 visual fields and FAF



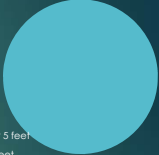
## Plaquenil Toxicity

- ▶ Hydroxychloroquine sulfate (Plaquenil) Risk Factors
  - ▶ Duration of use - > 5 years
  - ▶ Cumulative dose -> 1000g (total)    1000g/0.4g = 2,500 days or 7 years
  - ▶ Daily dose –
    - ▶ > 400 mg/day (200 mg PO BID)
    - ▶ > 6.5 mg/kg ideal body weight
  - ▶ Age – Elderly
  - ▶ Systemic disease – Kidney or liver disease
  - ▶ Ocular disease – Retinal disease or maculopathy



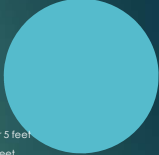
## Plaquenil Toxicity

- ▶ Hydroxychloroquine sulfate (Plaquenil) Risk Factors
  - ▶ Daily dose –
    - ▶ > 400mg/day
    - ▶ Real body weight - > 5 mg/kg
    - ▶ Ideal body weight - > 6.5 mg/kg
      - ▶ Women – 100 lb for first 5 feet, plus 5 lb for every inch of height over 5 feet
      - ▶ Men – 110 lb for first 5 feet, plus 5 lb for every inch of height over 5 feet

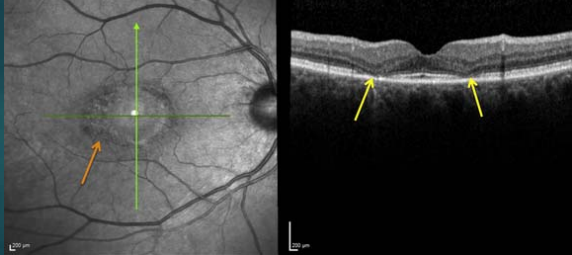


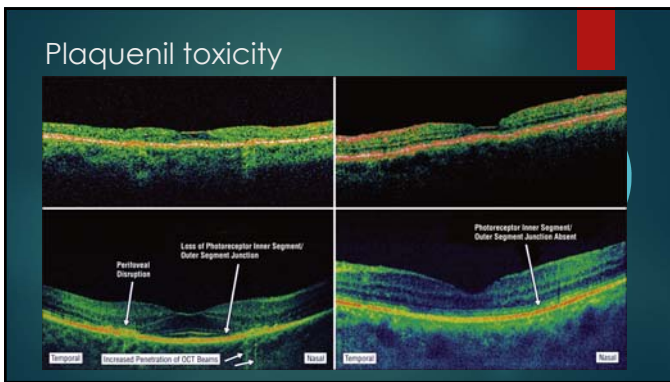
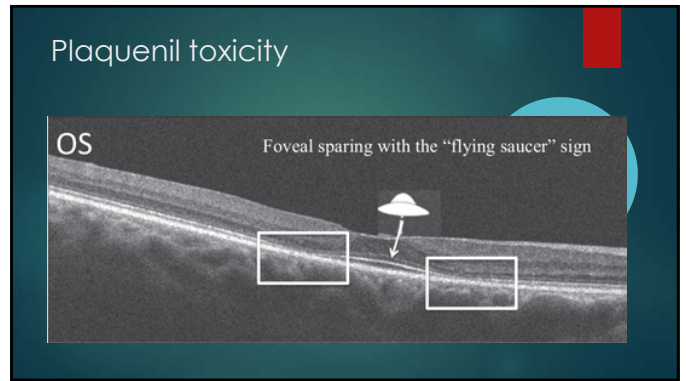
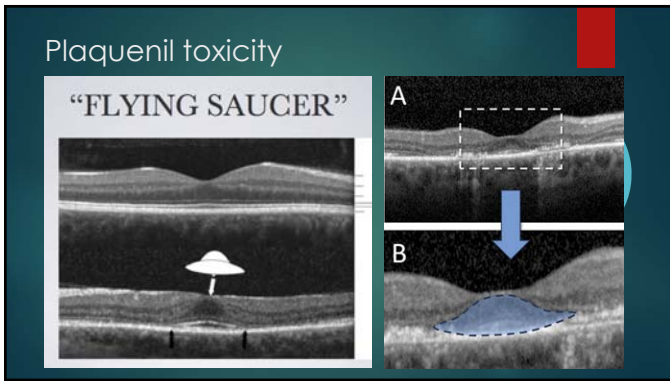
## Plaquenil Toxicity

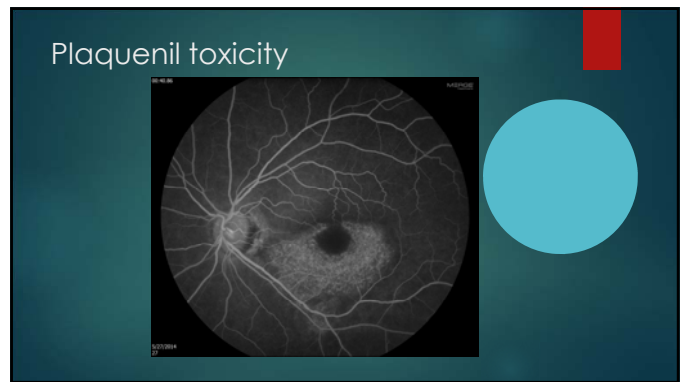
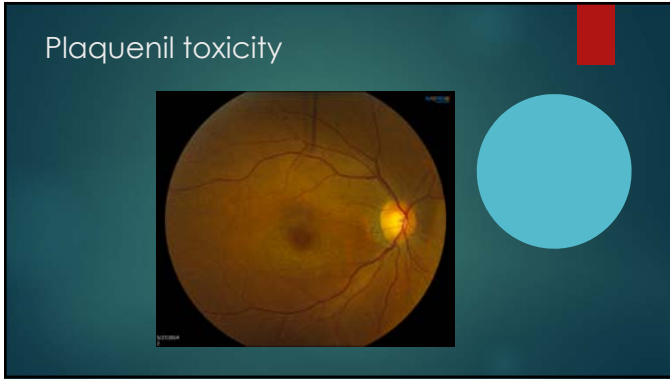
- ▶ Hydroxychloroquine sulfate (Plaquenil) Risk Factors
  - ▶ Daily dose –
    - ▶ > 400mg/day
    - ▶ Real body weight - > 5 mg/kg
    - ▶ Ideal body weight - > 6.5 mg/kg
      - ▶ Women – 100 lb for first 5 feet, plus 5 lb for every inch of height over 5 feet
      - ▶ Men – 110 lb for first 5 feet, plus 5 lb for every inch of height over 5 feet
- ▶ Many 5' 5" rheumatoid patients are very thin, under their "ideal" body weights and are getting overdosed



## Plaquenil toxicity

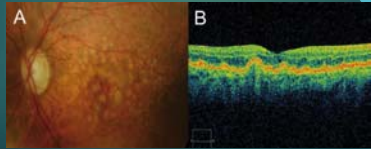




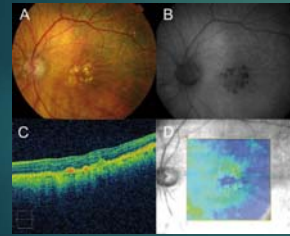


## Macular degeneration

- ▶ Age-related macular degeneration: Drusen, RPE changes, rule-out net
- ▶ Visual loss in dry ARMD is due to localized thinning of the photoreceptor layer immediately above the drusen
- ▶ SD-OCT instruments can accurately distinguish the presence and size of drusen and RPE changes, making it possible to differentiate the different retinal layers.



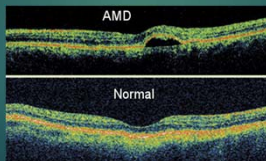
## Macular degeneration



- (A) Photography: Central hard drusen surrounded by areas of RPE atrophy
- (B) Autofluorescence image: hypofluorescence area corresponding to atrophic areas of the RPE
- (C) OCT: Two hyperreflective points corresponding to hard drusen
- (D) OCT infrared image

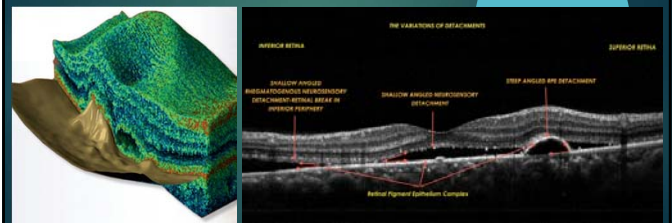
## Macular degeneration

- ▶ Because of the widespread use of OCT, the use of fluorescein angiography has dropped to second place in routine consultations
- ▶ FA is still an essential exam for studying CNV in patients with AMD, and FA and ICGA are especially important in identifying occult disease.



## Macular degeneration

- ▶ The main signs of CNV activity by OCT are the presence of **intraretinal or subretinal fluid** and **RPE detachments and tears**.



## Macular degeneration

- ▶ OCT is fundamental in the management of macular degeneration
- ▶ Since the introduction of PDT as an antiangiogenic agent a decade ago, OCT has provided information on the activity of neovascular membranes and determines the need to establish treatment, treatment response, and early signs of recurrence or resolution.
- ▶ Several multicenter studies were designed to evaluate treatment protocols of antiangiogenic therapies that **rely on OCT as the main criteria for retreatment**.

## Macular degeneration

- ▶ The injection protocols established in multicenter phase III studies of Lucentis for neovascular AMD, the ANCHOR and MARINA trials, consisted of **monthly intravitreal injections for 2 years for all study eyes** that resulted in substantial gains in VA in various intermediate controls and at the final examination. However, the dose of 24 injections carried a human and economic burden that made it difficult and impractical to administer.
- ▶ In phase I and II studies of Lucentis, before these studies, an extension study was conducted in which administration of new additional doses were left to the **discretion of the investigator** based on the presence of diffusion on FA or intraretinal or subretinal fluid on OCT. This subanalysis showed that **often the presence of retinal fluid could be detected much earlier by OCT than FA**, leaving the door open for a greater role of OCT in treatment.



### Macular degeneration "Treat and Observe" dosing

- ▶ **Three monthly loading doses**, monthly anti-VEGF injections are administered for 2 years according to the following criteria:
  1. Decrease of 5 letters of vision and fluid on **OCT**
  2. Increase of 100 microns in central retinal thickness on **OCT**
  3. Macular hemorrhage
  4. Classic CNV in emerging FA
  5. Persistent fluid on **OCT** 1 month after the last injection
- ▶ VA results were similar to monthly anti-VEGF for 2 years, but required significantly fewer injections (5.6 vs 12 in 1<sup>st</sup> year, 9.9 vs 24 total).
- ▶ The good results with fewer injections based on OCT led to **inclusion of OCT as a primary criteria** in new multicenter studies such as the SAILOR or SUSTAIN studies.

### Macular degeneration "Treat and Extend" dosing

- ▶ **Three monthly loading doses**, which are continued monthly until
  - Stable visual acuity
  - Absence of macular hemorrhage
  - Dry OCT
- ▶ Patients then continue to receive regular maintenance injections at increasing intervals, extended to 6 weeks. Visual acuity, clinical findings, and OCT changes are recorded again and patients receive an injection regardless of the presence or absence of disease activity.
- ▶ If stable, interval to the next visit (and injection) is extended to 7-8 weeks.
- ▶ If evidence of renewed disease activity, interval is shortened.
- ▶ Max interval between injection and examination typically 8-9 weeks.

### Dry macular degeneration

### Wet macular degeneration

OCT visualizes components of the neovascular membrane, retinal pigment epithelial detachment (PED), detachment of the neuroepithelium (NED), intraretinal fluid, and subretinal hemorrhage.

Picture D:  
 Drusenoid RPE detachments (Δ)  
 subretinal hemorrhage (+)  
 dense particles in subretinal fluid (⊥)  
 intraretinal migration of RPE cells (>)

### Wet macular degeneration

### Wet macular degeneration

