Managing the Vitreomacular Interface

A Guide to VMA, VMT, Holes and ERM

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BIO:

Dr. Anna Bedwell is a Clinical Associate Professor at Indiana University School of Optometry. She completed her optometry degree from IU in 2010 and a residency at the San Francisco VA in 2011. She is a fellow of the American Academy of Optometry and a member of the American Optometric Association. Dr. Bedwell, also, holds fellowship in the Optometric Retina Society, where she currently serves as the editor of their quarterly newsletter.

Disclosures: None

Vitreous Anatomy

- Composition = 98-99% water
  - the rest = 2 main macromolecules: collagen, hyaluronic acid
- 3 parts:
  - Central core
  - Cortex – dense collagen matrix
    - Collagen provides shape, hyaluronic acid provides elasticity
    - 100 microns thick
  - Posterior hyaloid
    - Thin membrane between cortex and internal limiting membrane of the retina
    - glue-like attachment to the ILM made up of fibronectin, laminin

Vitreous Aging

- At age 9 or 10, the human vitreous gel begins to liquefy
- Liquefaction: occurs as collagen aggregates into bundles causing pockets of liquid (lacunae)
- By age 40 the vitreous is 80% gel/20% liquid
- By age 80 the vitreous is 50% gel/50% liquid

Posterior Vitreous Detachment

- Detachment of the posterior cortex of the vitreous from the internal limiting membrane of the retina
- PVD occurs as vitreous liquefaction ↑ and vitreoretinal adherence ↓
- Attachment Sites:
  - Ora (strongest)
  - Post lens capsule
  - Optic disc
  - Macula
  - Vasculature (weakest)

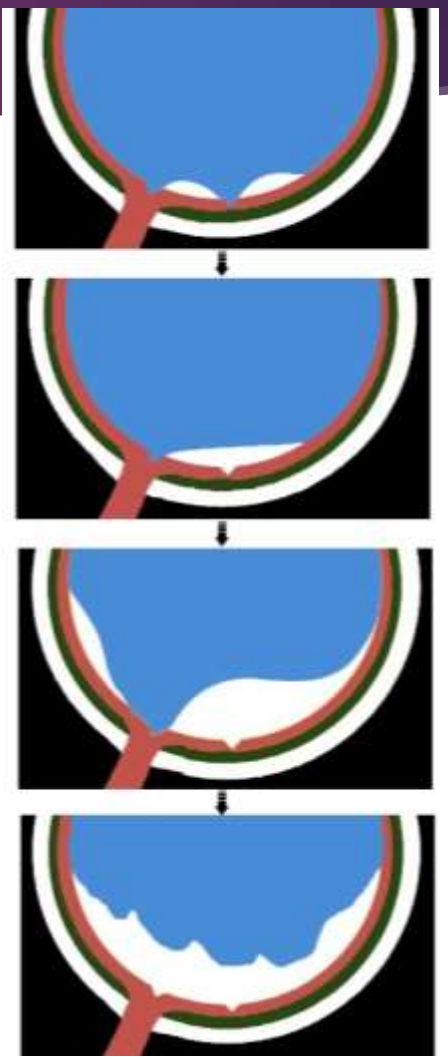
Stages of PVD

Perifoveal separation with vitreofoveal adhesion

Complete vitreomacular separation

Complete vitreoretinal interface separation except at the optic disc

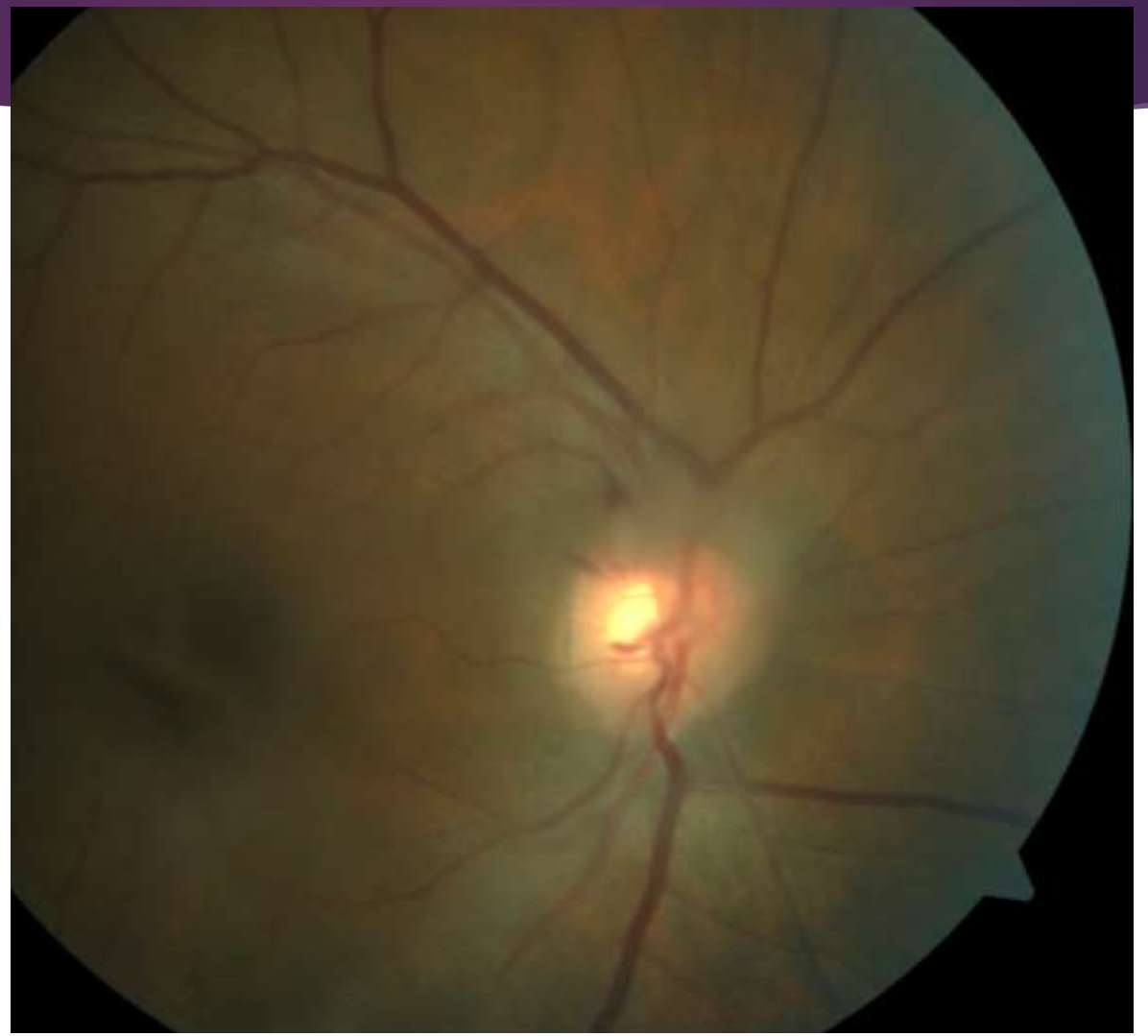
Complete PVD with Weiss ring



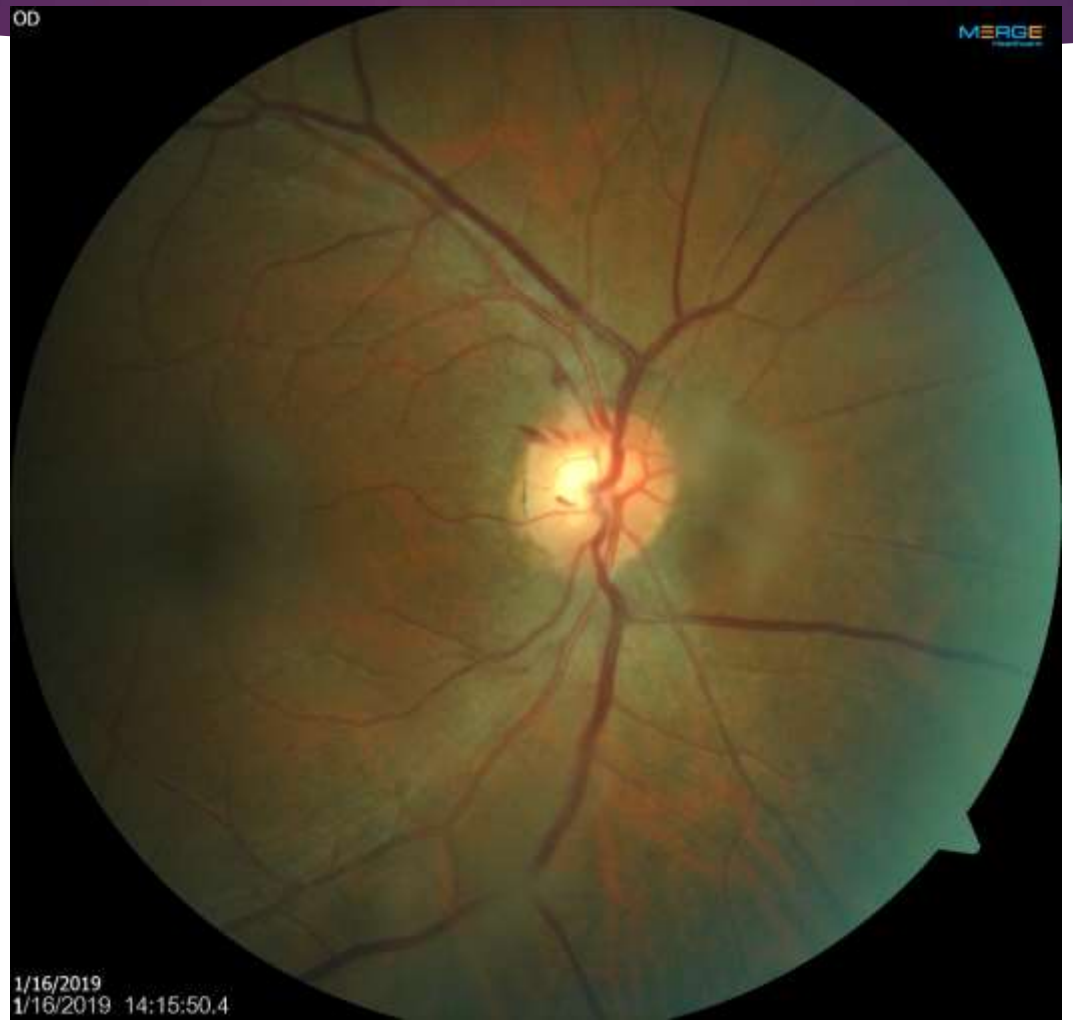
Blame it on the Vitreous

- Anomalous PVD = gel liquefaction moves faster than vitreoretinal dehiscence
- Complications:
  - Periphery – breaks, detachment, WWP
  - Vasculature – I/R hemorrhages, vitreous hemorrhage, aggravate neovascularization
  - Optic disc – aggravate NVD, vitreo-papillary traction syndrome
  - Macula – contributes to DME and exudative AMD, vitreomacular interface disorders

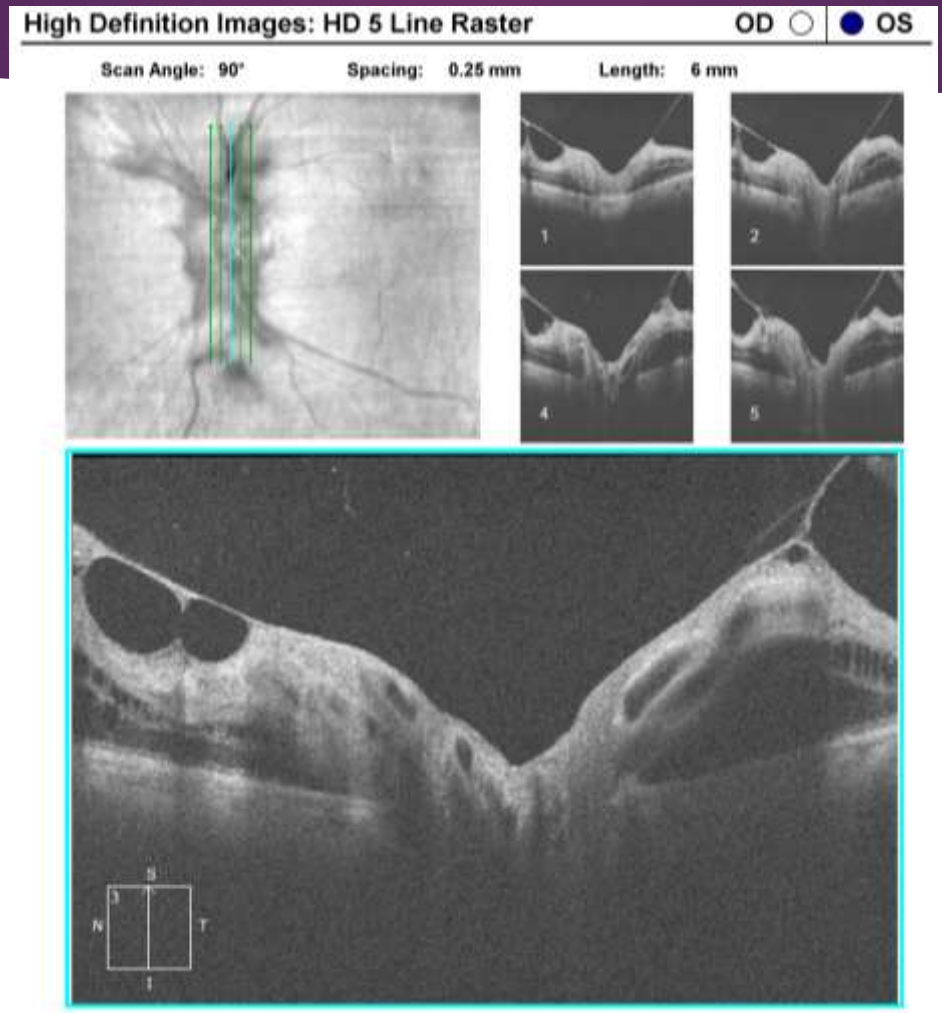
Vitreo-papillary traction

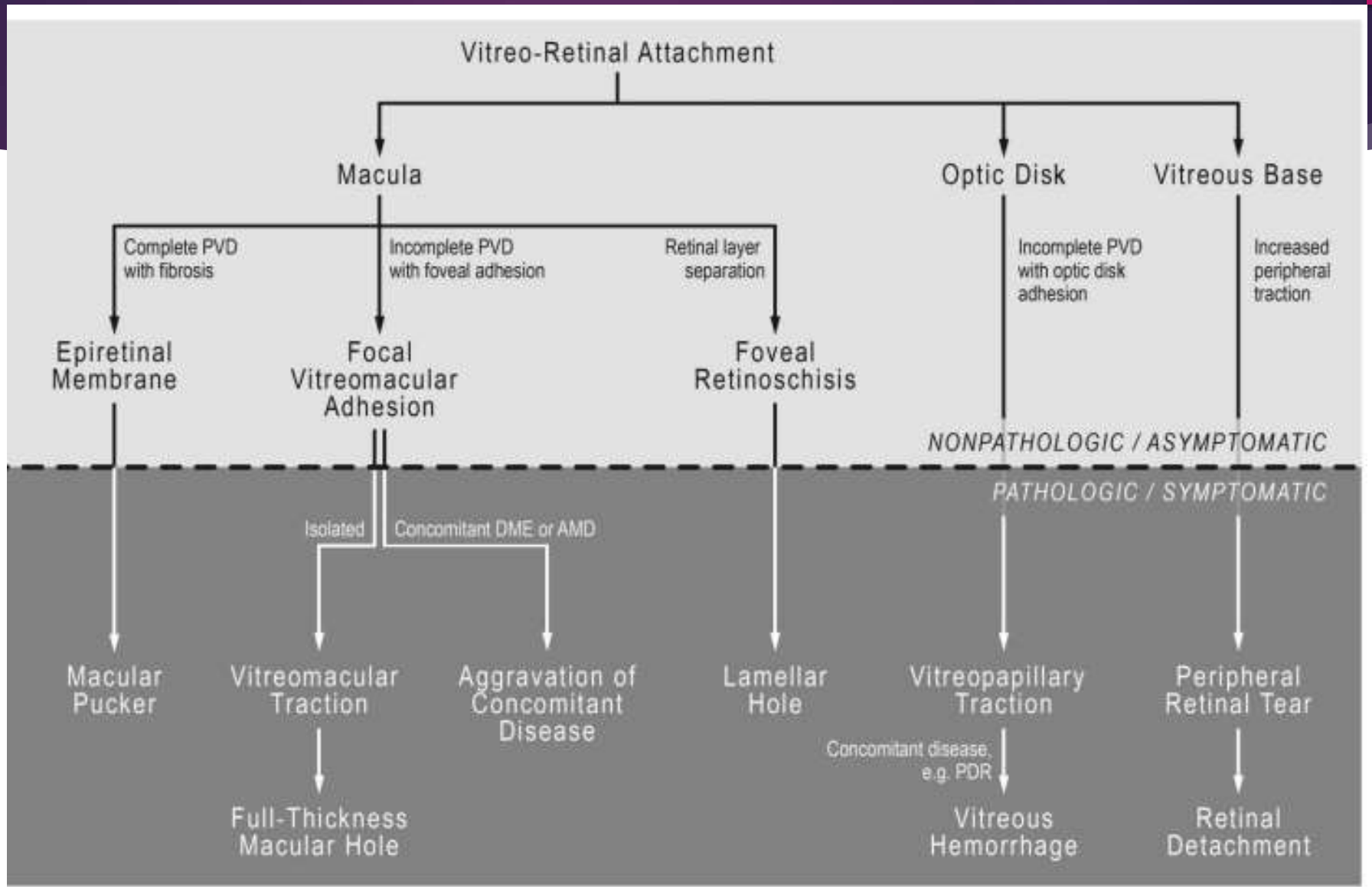


Vitreo-papillary traction (one week later, released)



Vitreo-papillary traction





Stalmans P. Retina. 2013

Responsible for defining VMI disorders

The International Vitreomacular Traction Study Group Classification of Vitreomacular Adhesion, Traction, and Macular Hole

Jay S. Duker, MD,[1] Peter K. Kaiser, MD,[2] Susanne Binder, MD,[3,4] Marc D. de Smet, MD,[5] Alain Gaudric, MD,[6] Elias Reichel, MD,[1] SriniVas R. Sadda, MD,[7] Jerry Sebag, MD,[7,8] Richard F. Spaide, MD,[9] Peter Stalmans, MD, PhD[10]

Objective: The International Vitreomacular Traction Study (IVTS) Group was convened to develop an optical coherence tomography (OCT)-based anatomic classification system for diseases of the vitreomacular interface (VMI).

Design: The IVTS applied their clinical experience, after reviewing the relevant literature, to support the development of a strictly anatomic OCT-based classification system.

Participants: A panel of vitreoretinal disease experts was the foundation of the International Classification System.

Methods: Before the meeting, panel participants were asked to review 11 articles and to complete 3 questionnaires. The articles were preselected based on searches for comprehensive reviews covering diseases of the VMI. Responses to questionnaires and the group's opinions on definitions specified in the literature were used to guide the discussion.

Main Outcome Measures: Optical coherence tomography-based anatomic definitions and classification of vitreomacular adhesion, vitreomacular traction (VMT), and macular hole.

Results: Vitreomacular adhesion is defined as perifoveal vitreous separation with remaining vitreomacular attachment and unperturbed foveal morphologic features. It is an OCT finding that is almost always the result of normal vitreous aging, which may lead to pathologic conditions. Vitreomacular traction is characterized by anomalous posterior vitreous detachment accompanied by anatomic distortion of the fovea, which may include pseudocysts, macular schisis, cystoid macular edema, and subretinal fluid. Vitreomacular traction can be subclassified by the diameter of vitreous attachment to the macular surface as measured by OCT, with attachment of 1500 μm or less defined as focal and attachment of more than 1500 μm as broad. When associated with other macular disease, VMT is classified as concurrent. Full-thickness macular hole (FTMH) is defined as a foveal lesion with interruption of all retinal layers from the internal limiting membrane to the retinal pigment epithelium. Full-thickness macular hole is primary if caused by vitreous traction or secondary if directly the result of pathologic characteristics other than VMT. Full-thickness macular hole is subclassified by size of the hole as determined by OCT and the presence or absence of VMT.

Conclusions: This classification system will support systematic diagnosis and management by creating a clinically applicable system that is predictive of therapeutic outcomes and is useful for the execution and analysis of clinical studies.

Financial Disclosure(s): Proprietary or commercial disclosure may be found after the references. *Ophthalmology 2013;120:2611-2619*

Vitreomacular Adhesion (VMA)

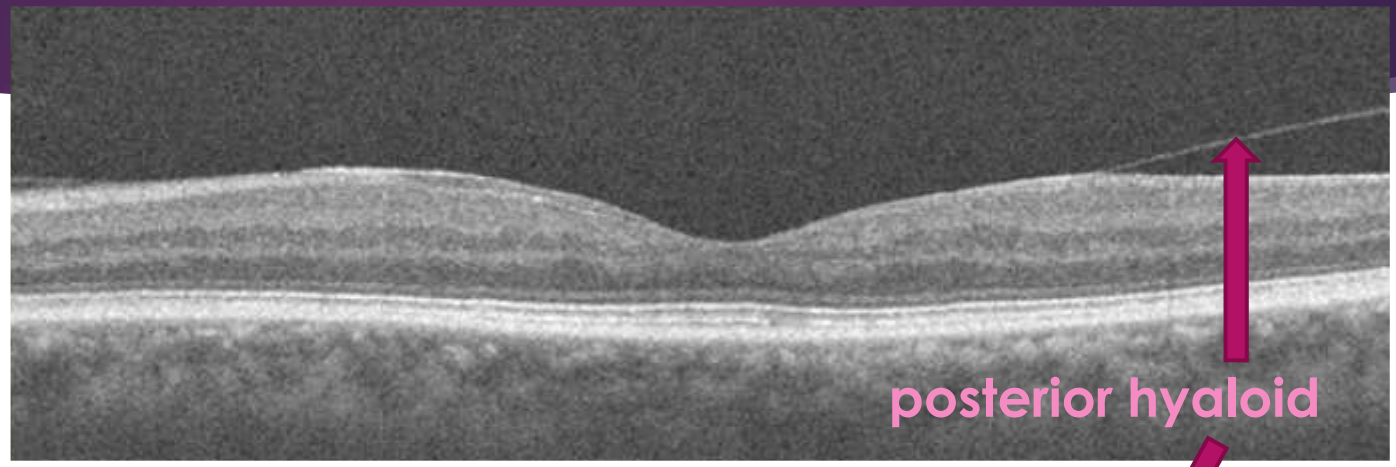
- Partial detachment of the vitreous in the perifoveal area without corresponding retinal abnormality (no change in retinal contour)
- Normal finding that occurs over the natural course of PVD

Focal: ≤1500 um

Broad: >1500 um

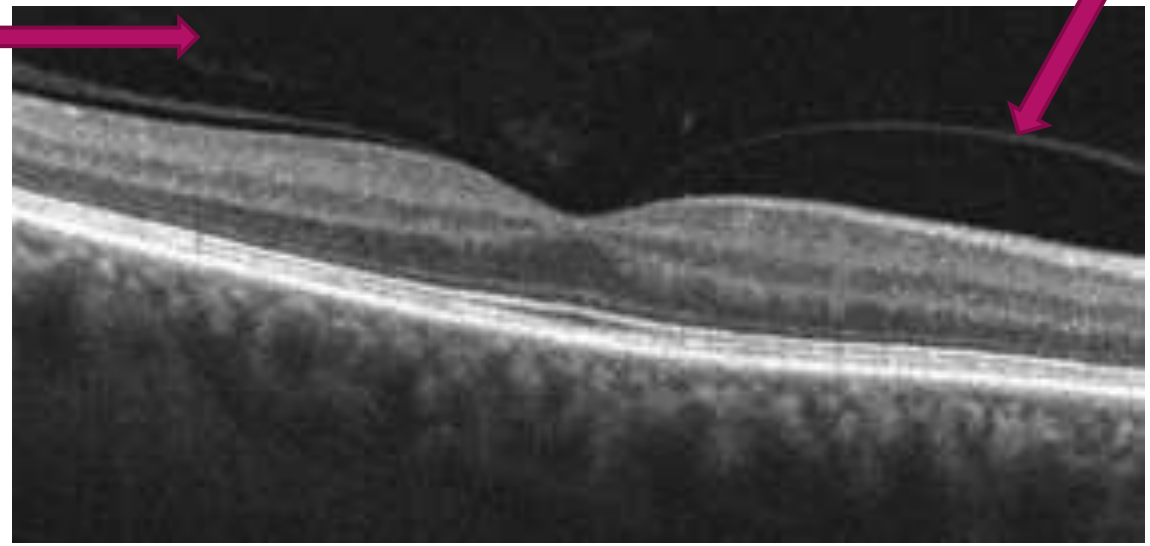
VMA

Broad



vitreous cortex

Focal



PREVALENCE OF VITREOMACULAR ADHESION IN PATIENTS WITHOUT MACULOPATHY OLDER THAN 40 YEARS

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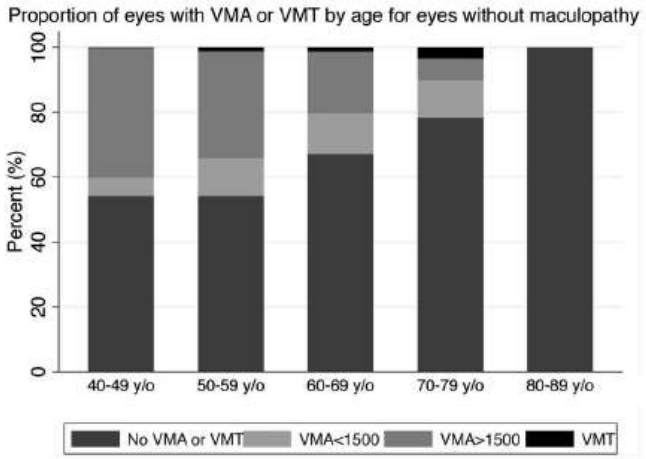
JOSEPH J. PIZZIMENTI, OD,‡ AVA K. BITTNER, OD, PhD* VAST Study Group

- 1,950 eyes: 38% had VMA and 1% had VMT
- VMA most often found in 40-49 age group
- Odds of VMA/VMT decreased by 7% with each year of age
- African Americans were less likely to have VMA/VMT than Caucasians



Retina 2017

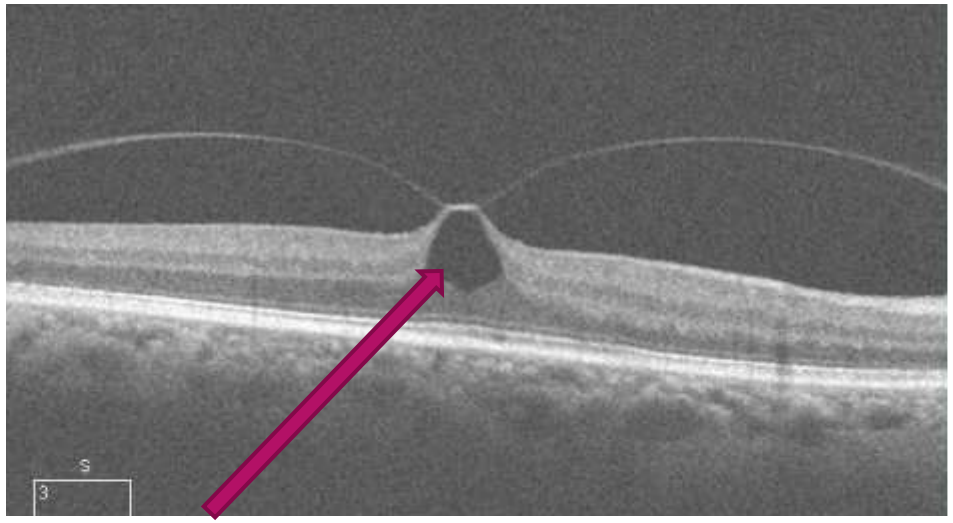
Vitreomacular Traction (VMT)

- Partial detachment of the vitreous in the perifoveal area with corresponding retinal abnormality
  - (ie: change in retinal contour, distortion, pseudocyst formation)
- No full thickness interruption of layers
- Can cause retinal thickening, schisis, pseudocyst formation, vascular leakage on FA or CME
- Sxs (if present): blur, metamorphopsia, micropsia, photopsias

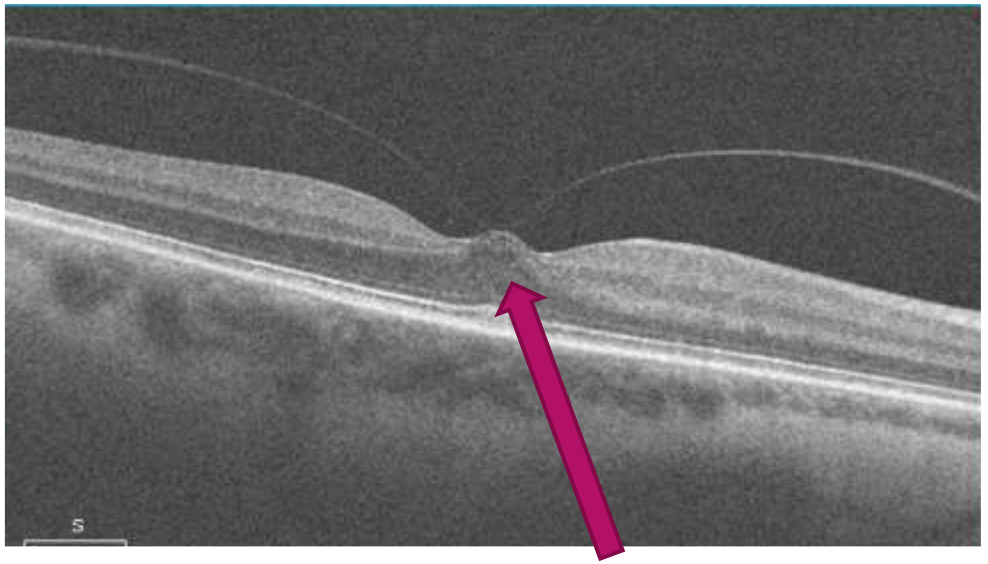
Focal: ≤1500 um

Broad: >1500 um

Focal VMT



Pseudocyst

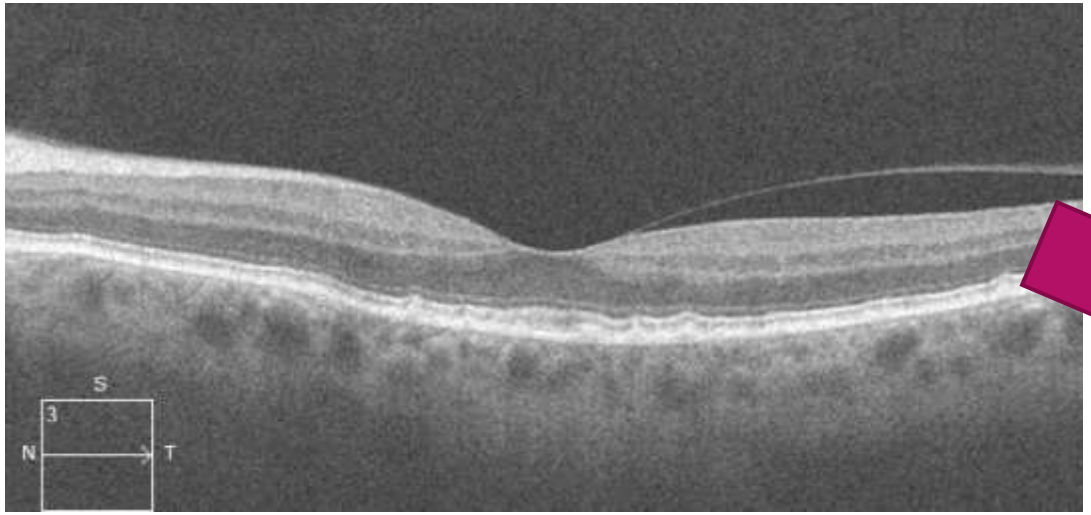


Disruption of foveal contour

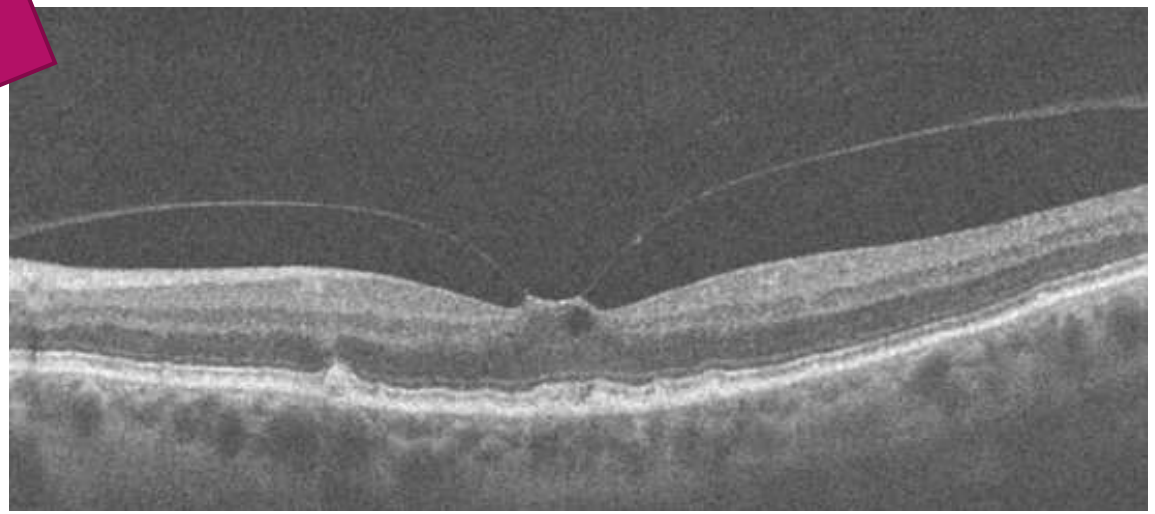
Very subtle clinical changes. Best appreciated on OCT.

VMT Example Timeline

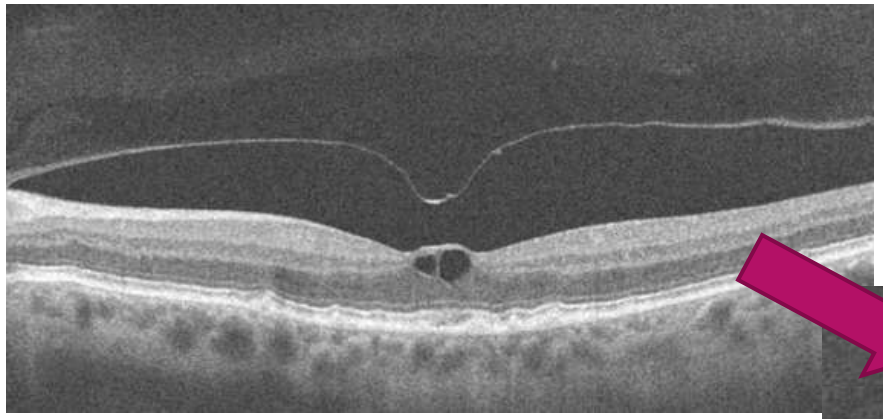
3/2015 VMA



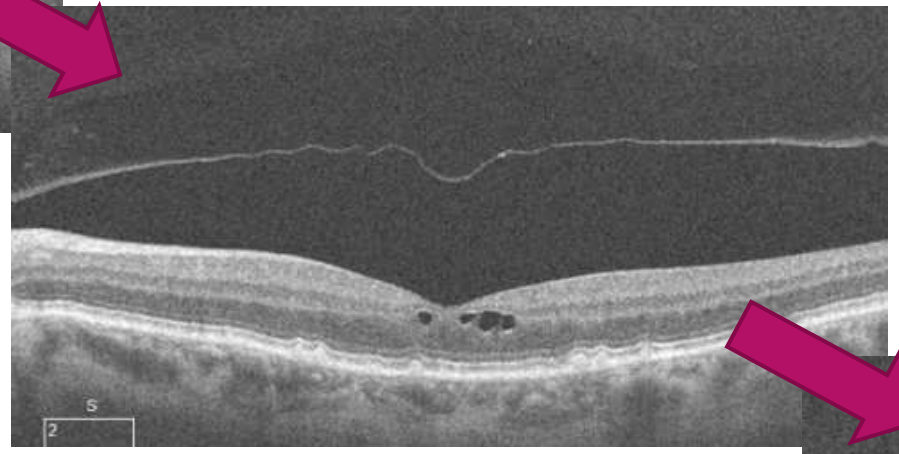
2/2016 Asymptomatic VMT



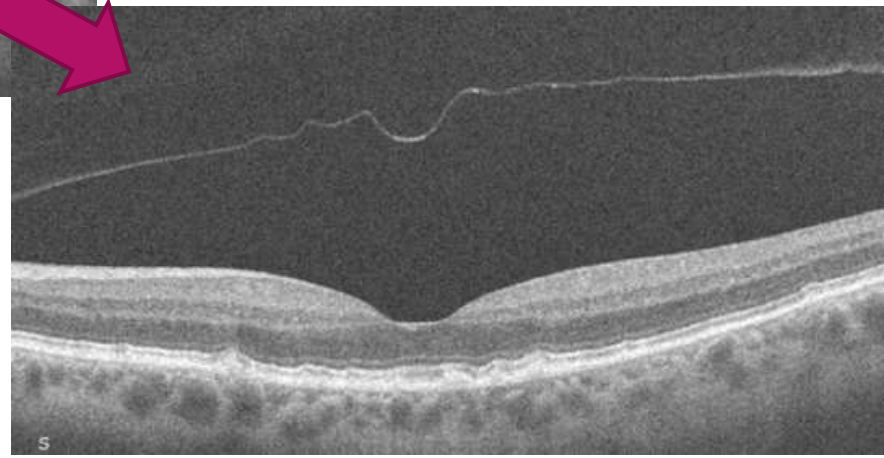
3/2016 VMT releases, notice the changes to the cortex



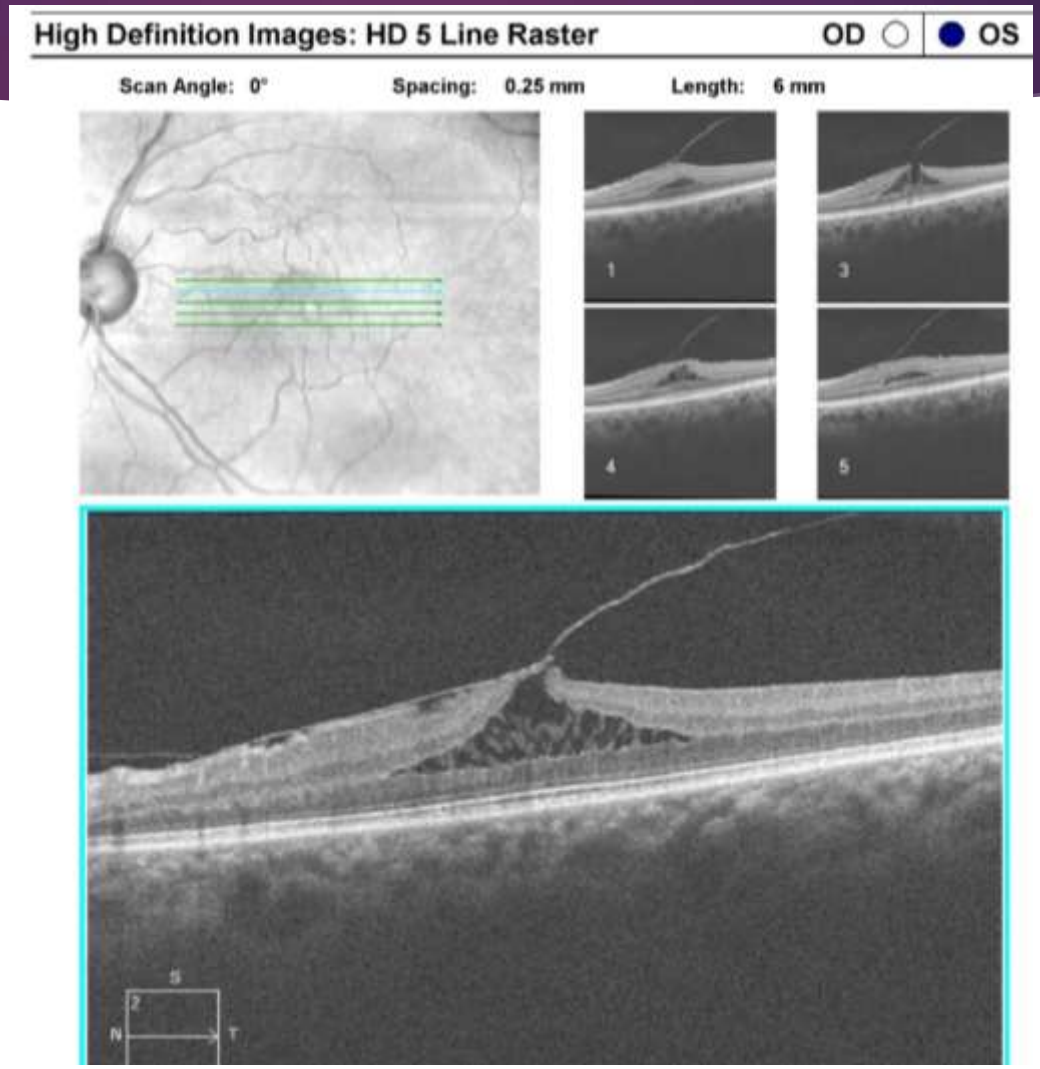
7/2016



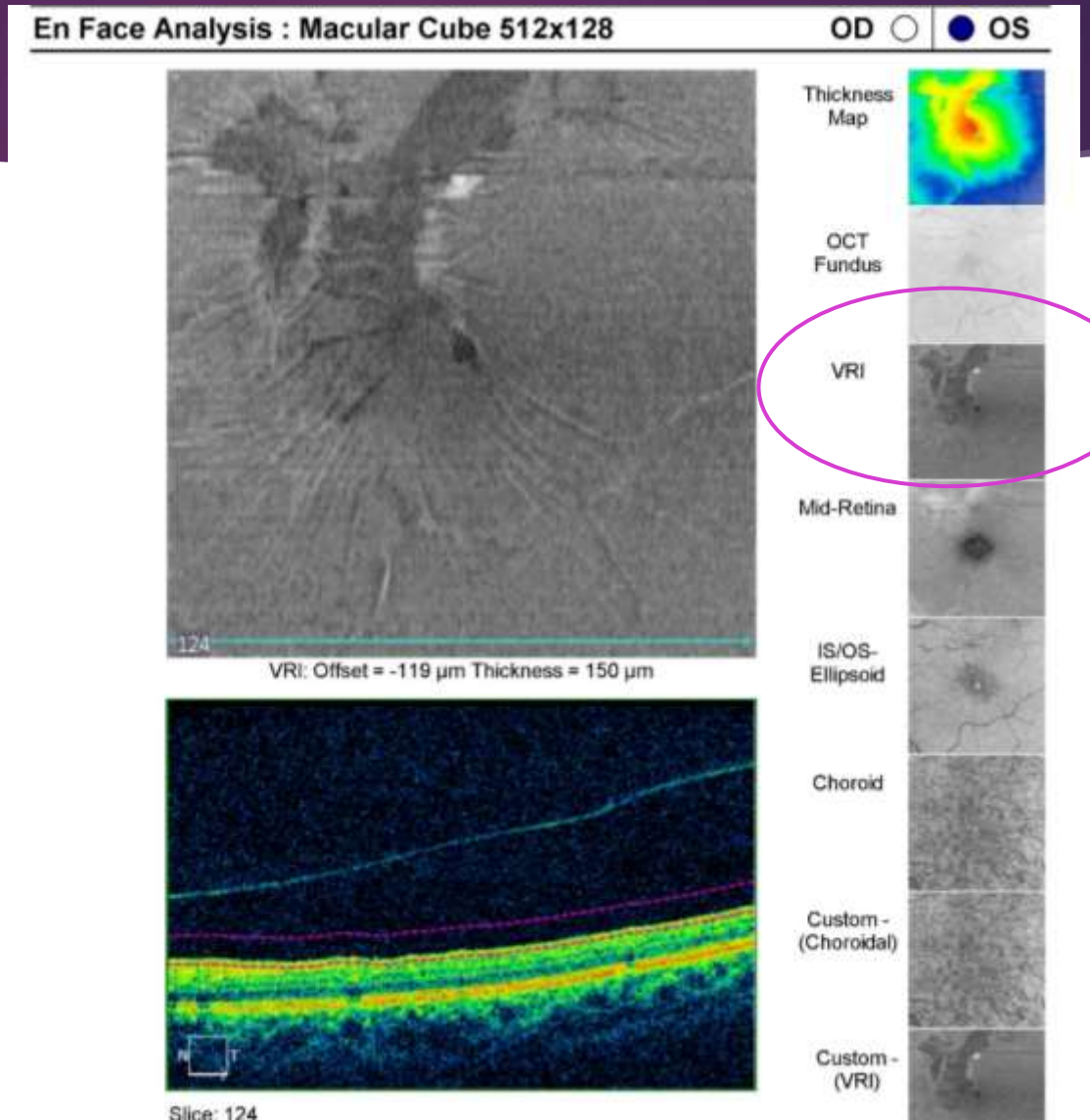
11/2016 cystic edema takes a few months to resolve



Broad VMT with ERM



En Face - ERM

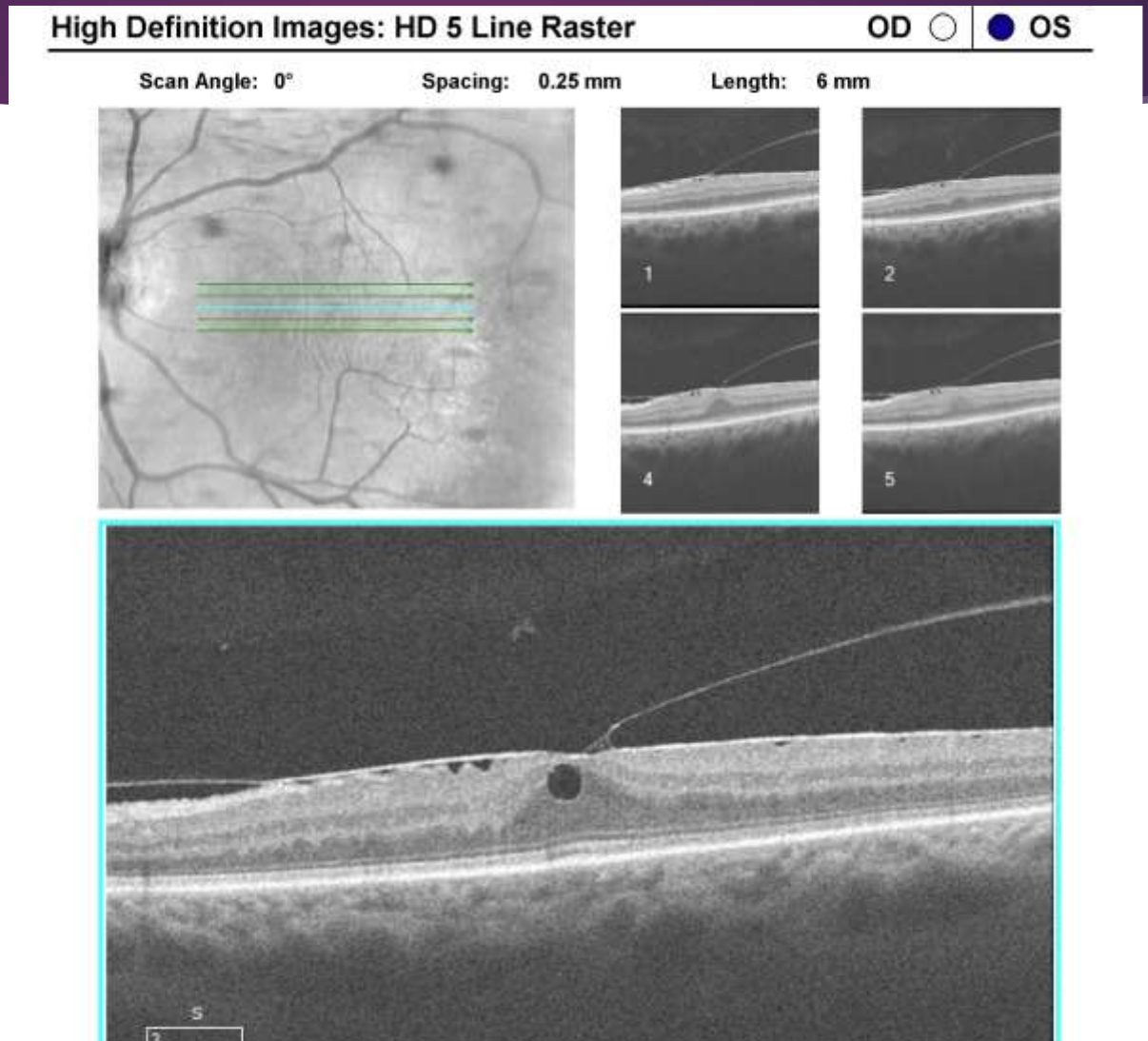


Can isolate to the vitreoretinal interface.

Broad VMT with ERM

Traction from two directions: anterior-posterior from VMT and posterior hyaloid and tangential traction from the ERM.

This patient is 20/20 asymptomatic.



Chronic broad VMT -> more likely to develop ERM

Management of VMA/VMT

VMA → no treatment necessary

Asymptomatic VMT → monitor for spontaneous resolution

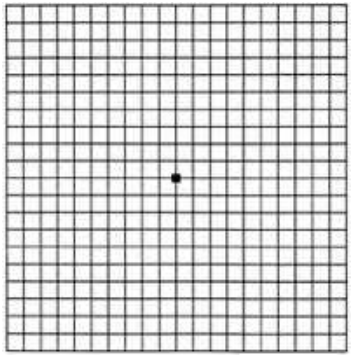
- Timeline for spontaneous resolution unclear
- ~5-12% of VMT will progress on to FTMH

Symptomatic VMT

- Refer to retina to consider ocriplasmin injection or PPV

  OR

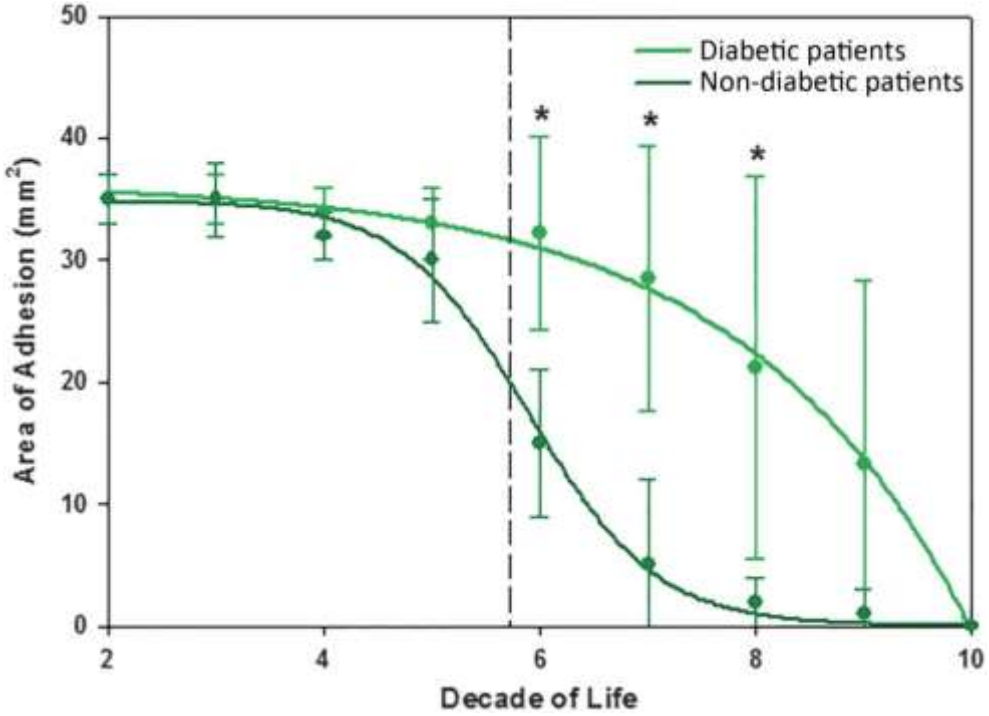
- If minimally symptomatic, can monitor closely for spontaneous resolution.



Relationship to Diabetes

Diabetics:

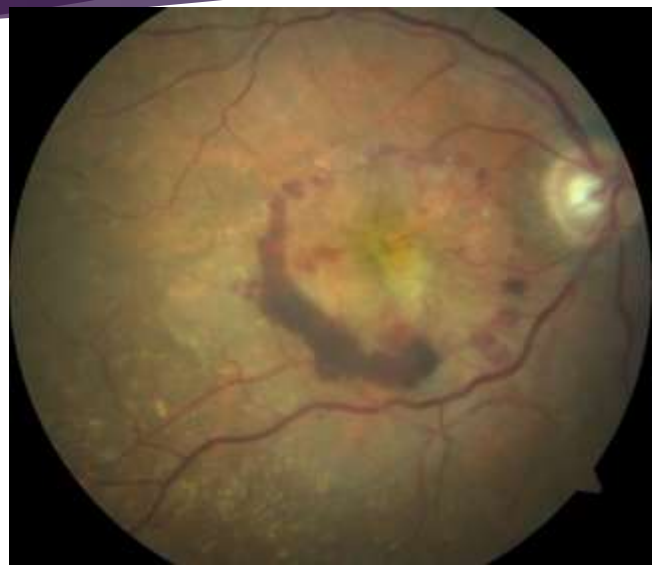
- Retain VMA longer
- Develop PVD at a later age
- Traction can antagonize DME
  - DME with concomitant ERM have poor response to anti-VEGF tx



Nesmith, BL. *Retina* 2017

VMA/VMT and Neovascular AMD

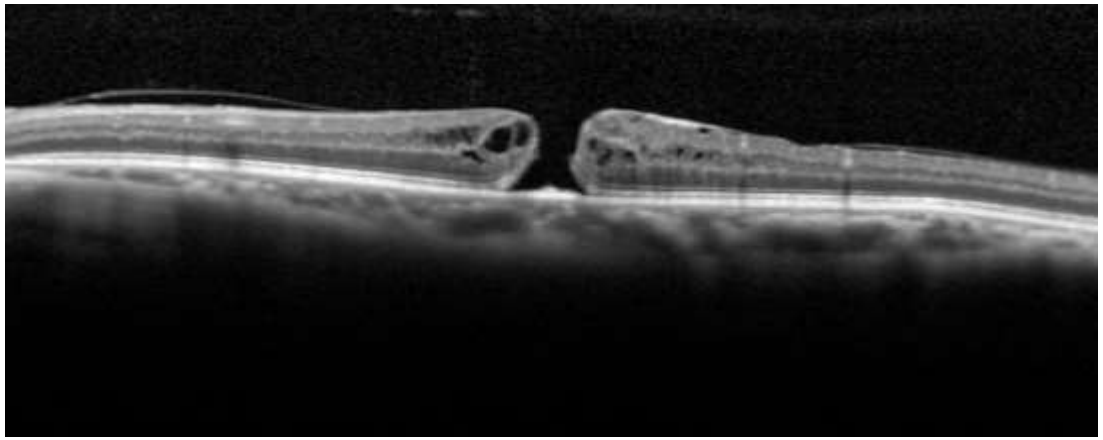
- VMA or VMT can decrease the effectiveness of anti-VEGF treatment in patients with neovascular AMD
  - worse effect earlier in treatment, less so at 12 months out as VMA/VMT was more likely to naturally release



Xie P, et al. Br J Ophthalmol 2017

Full Thickness Macular Hole

- Reddish, round lesion at fovea
- OCT: anatomic defect in the fovea with interruption of all neural retinal layers from ILM to RPE
  - Hourglass shape
- +/- vitreous attachment
- Primary v. Secondary
- F>M
- Fellow eye at increased risk
  - 10-15%



Full Thickness Macular Hole

- Classification:
  - Small: <250 um
  - Medium: 250-400 um
  - Large: > 400 um
- Measure with calipers the smallest width between sides
- Also note +/- VMT
- Rare for spontaneous closure
  - 71% of small holes progress

Treatment:
Small: vitrectomy (almost 100% success), ocriplasmin injection (good)
Medium: vitrectomy (>90% success), ocriplasmin injection (ok)
Large: vitrectomy (high closure rates w/ ILM peel)

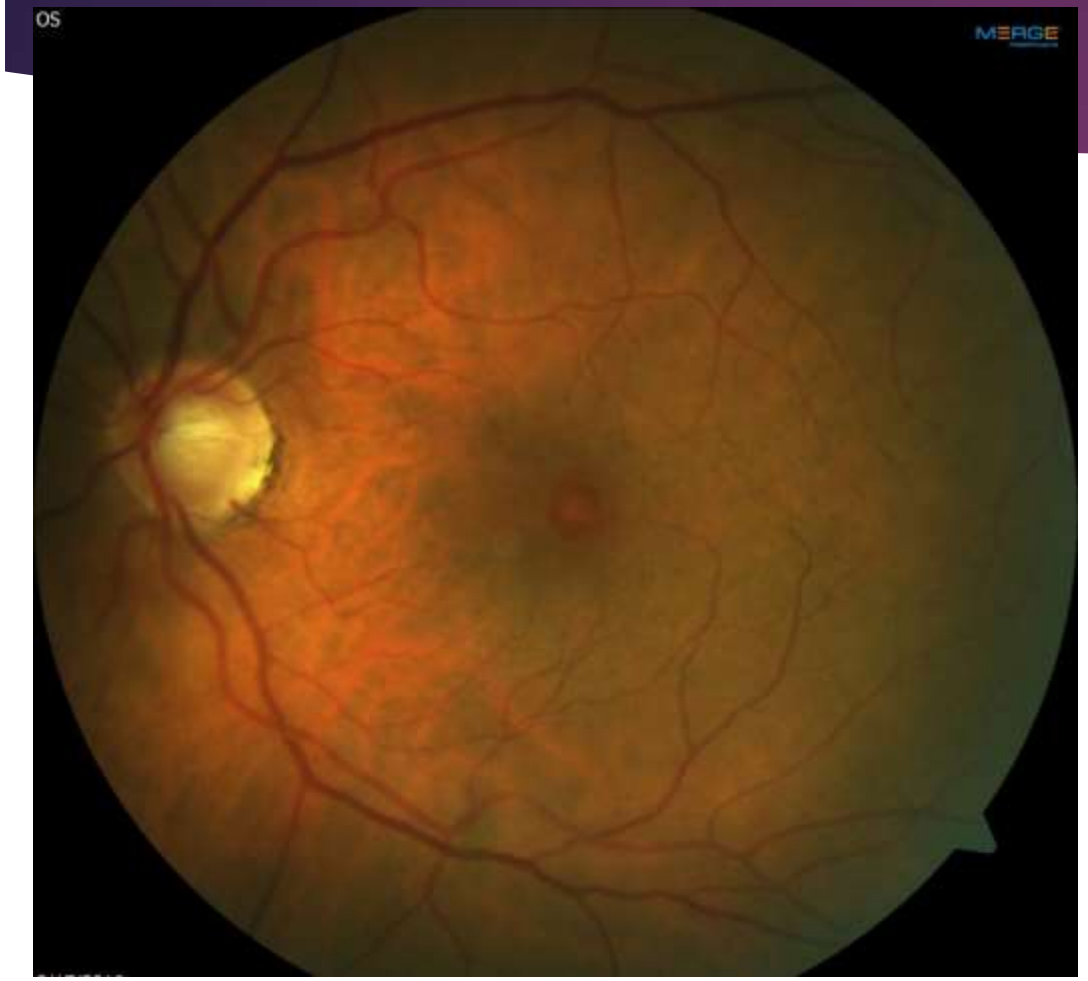
Table 2. Correlation between Commonly Used Clinical Macular Hole Stages and the International Vitreomacular Traction Study Classification System for Vitreomacular Adhesion, Traction, and Macular Hole

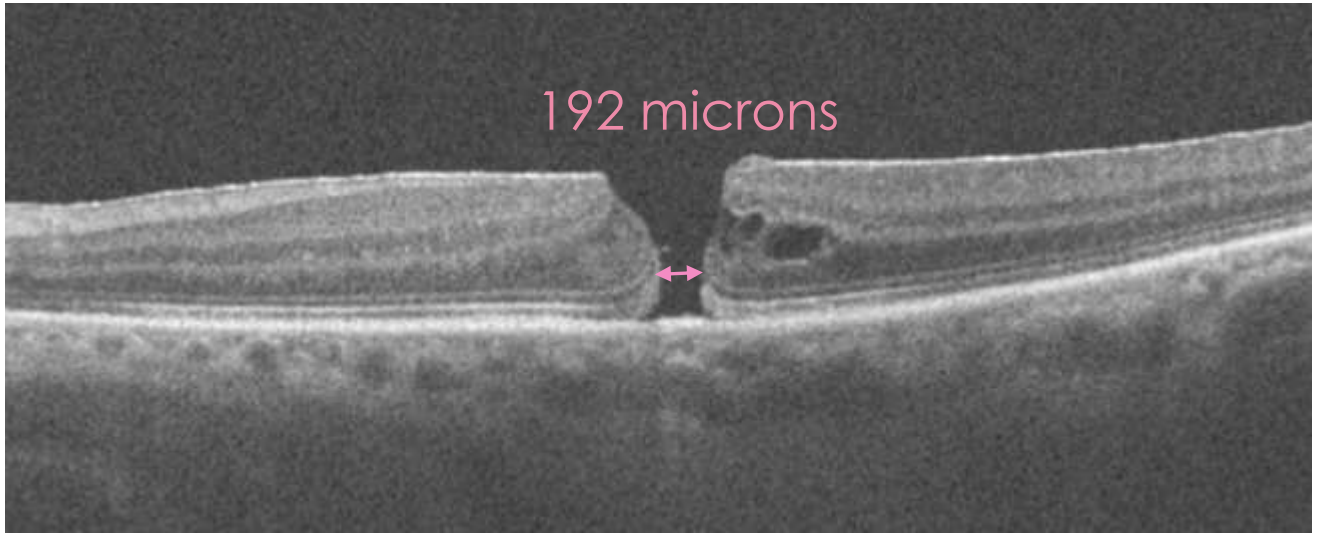
Full-Thickness Macular Hole Stages in Common Use	International Vitreomacular Traction Study Classification System
Stage 0	VMA
Stage 1: impending macular hole	VMT
Stage 2: small hole	Small or medium FTMH with VMT
Stage 3: large hole	Medium or large FTMH with VMT
Stage 4: FTMH with PVD	Small, medium, or large FTMH without VMT

FTMH = full-thickness macular hole; PVD = posterior vitreous detachment; VMA = vitreomacular adhesion; VMT = vitreomacular traction.

Old classification vs. New classification

FTMH - small





Treated successfully with vitrectomy, peel and gas.

FTMH - medium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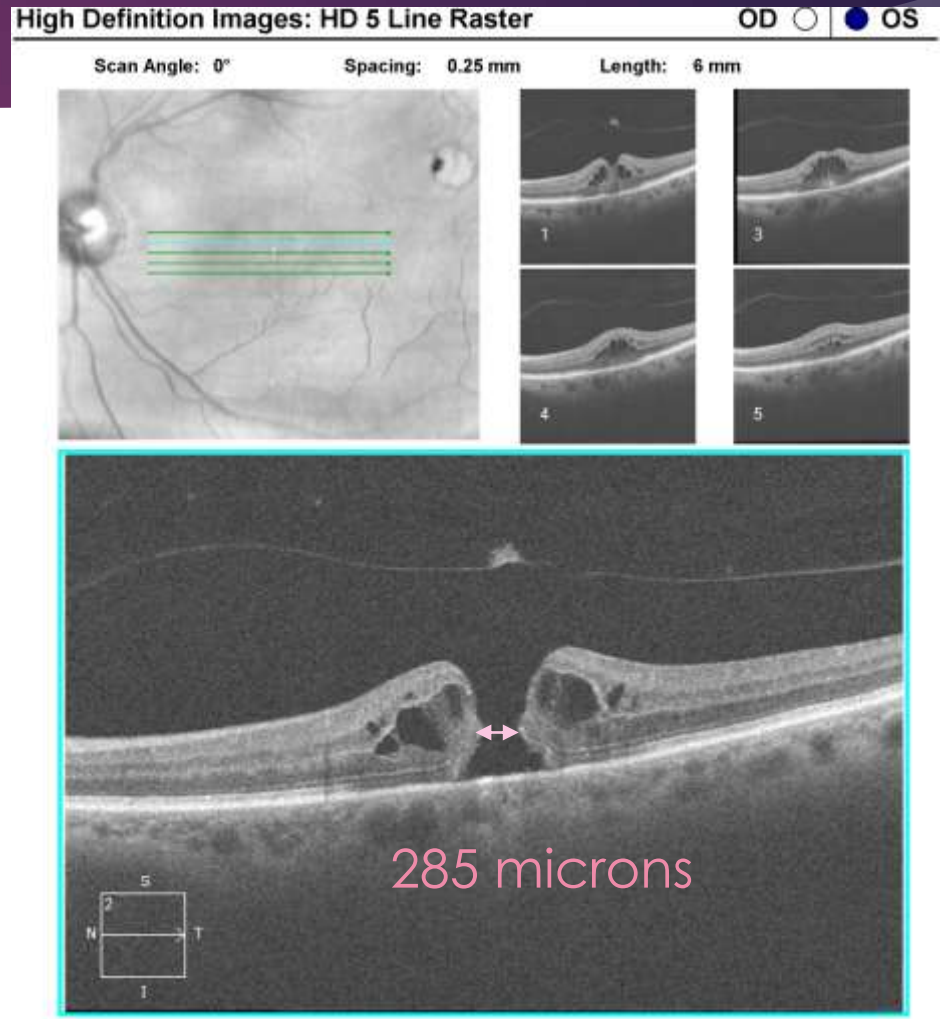
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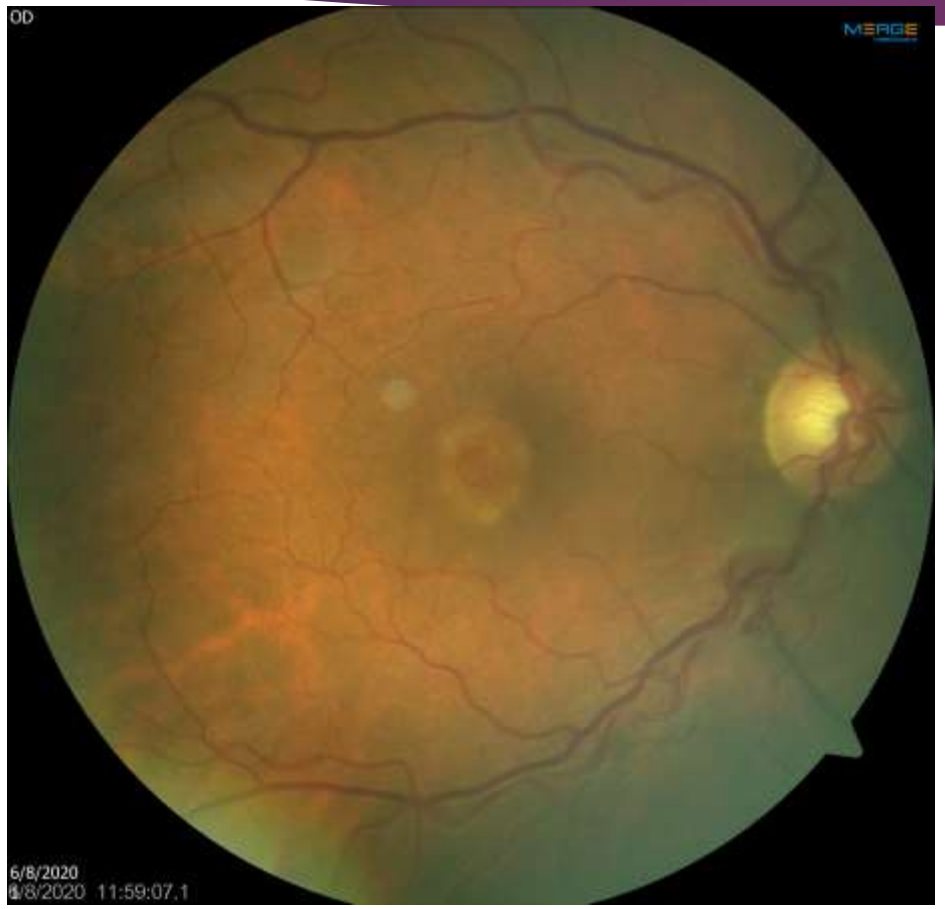
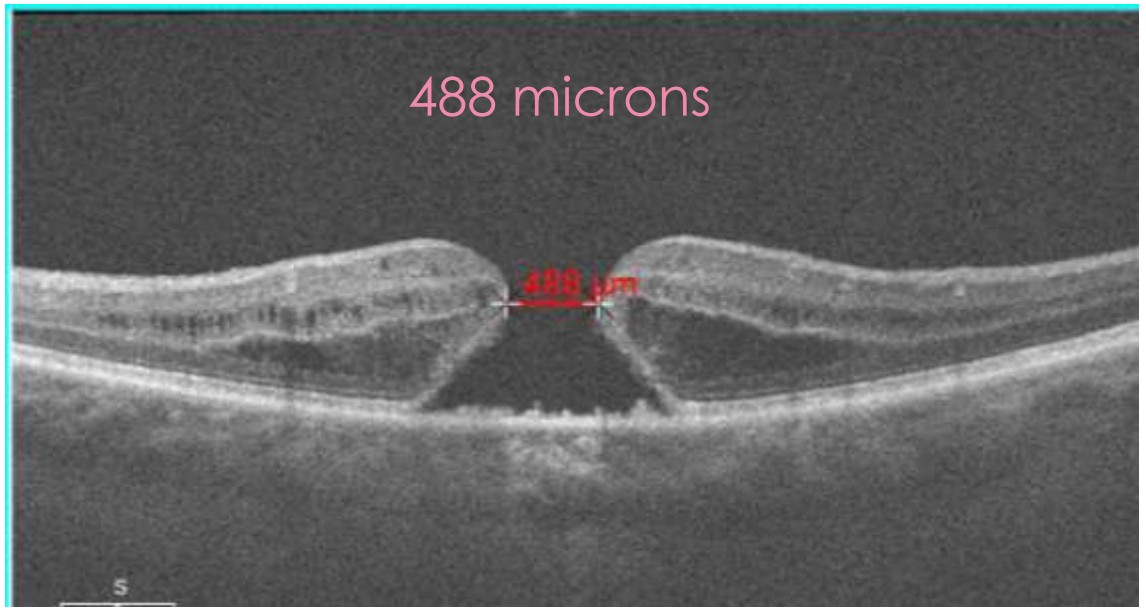
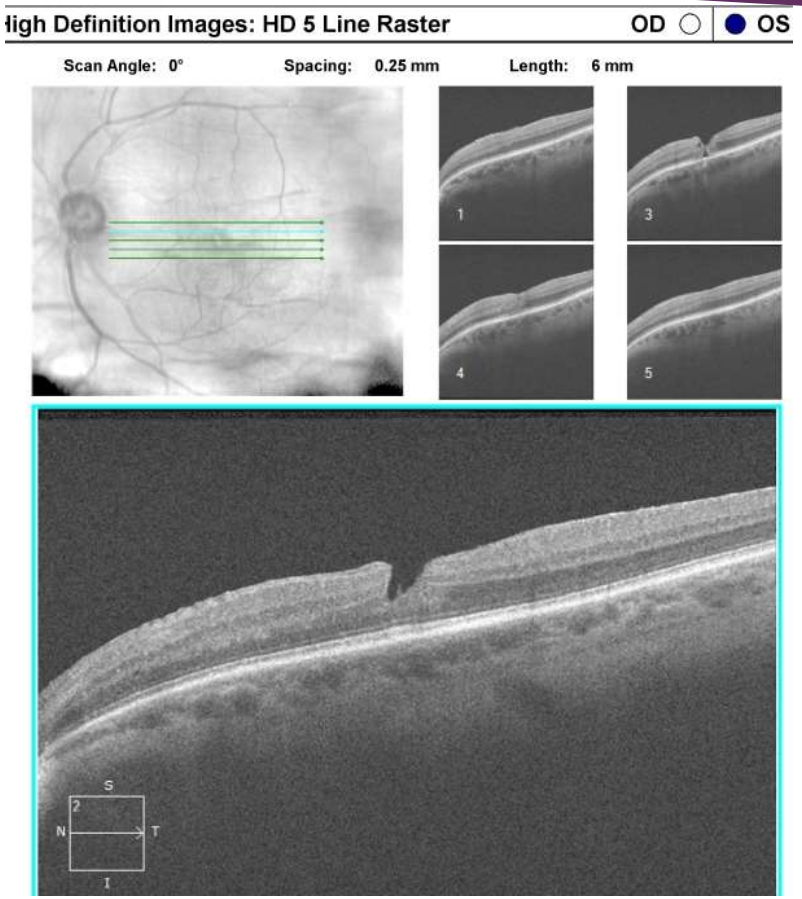
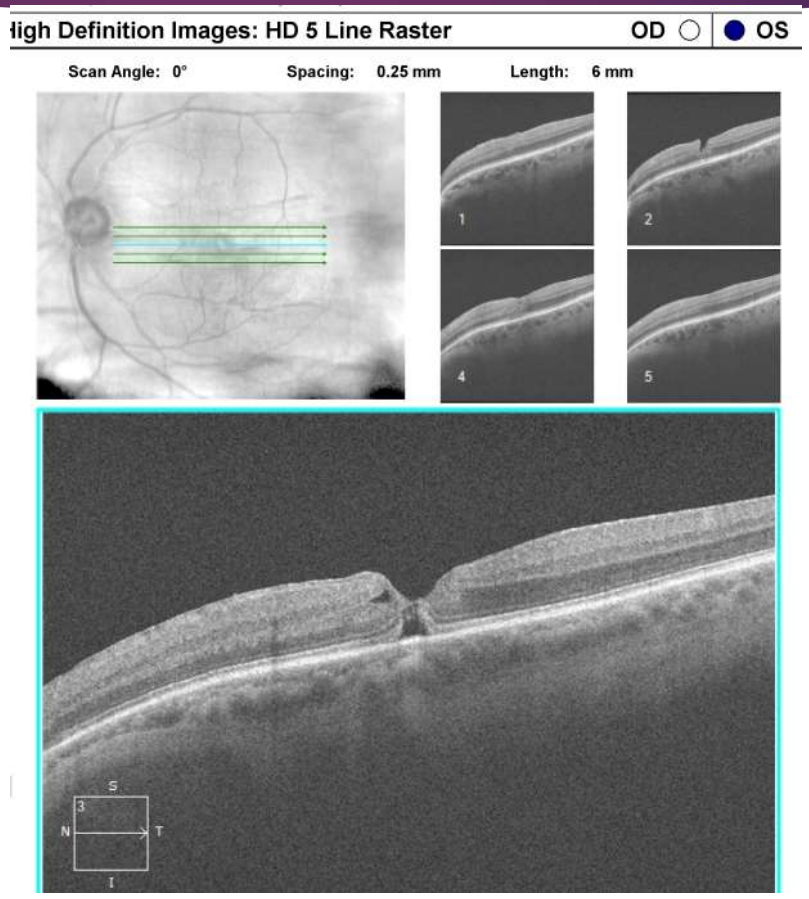
FTMH – large/chronic

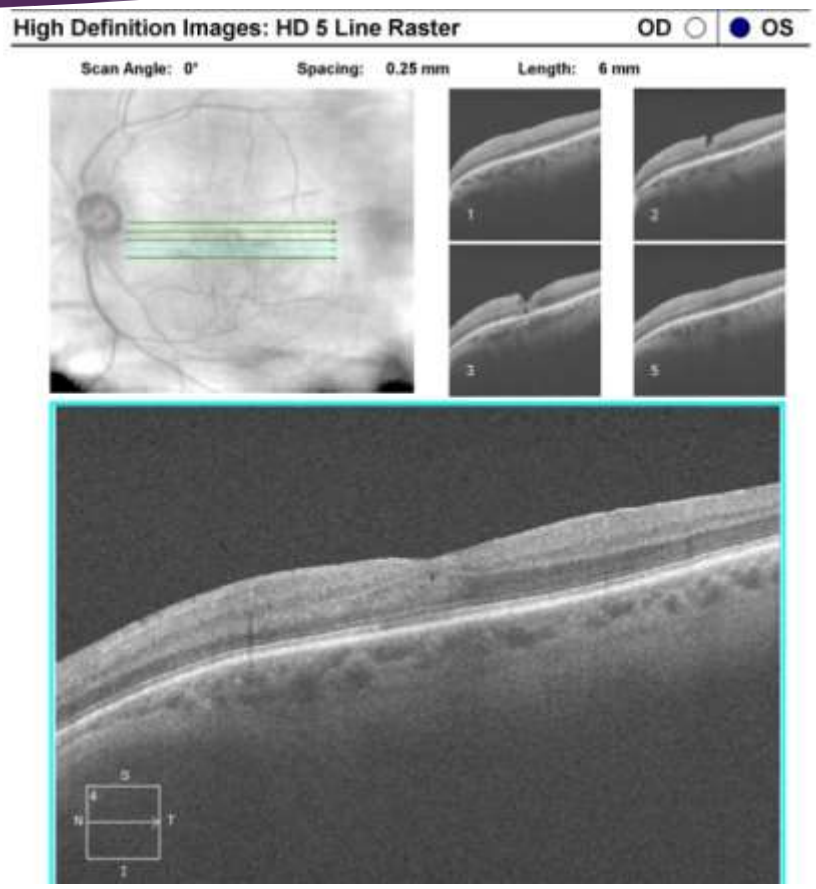




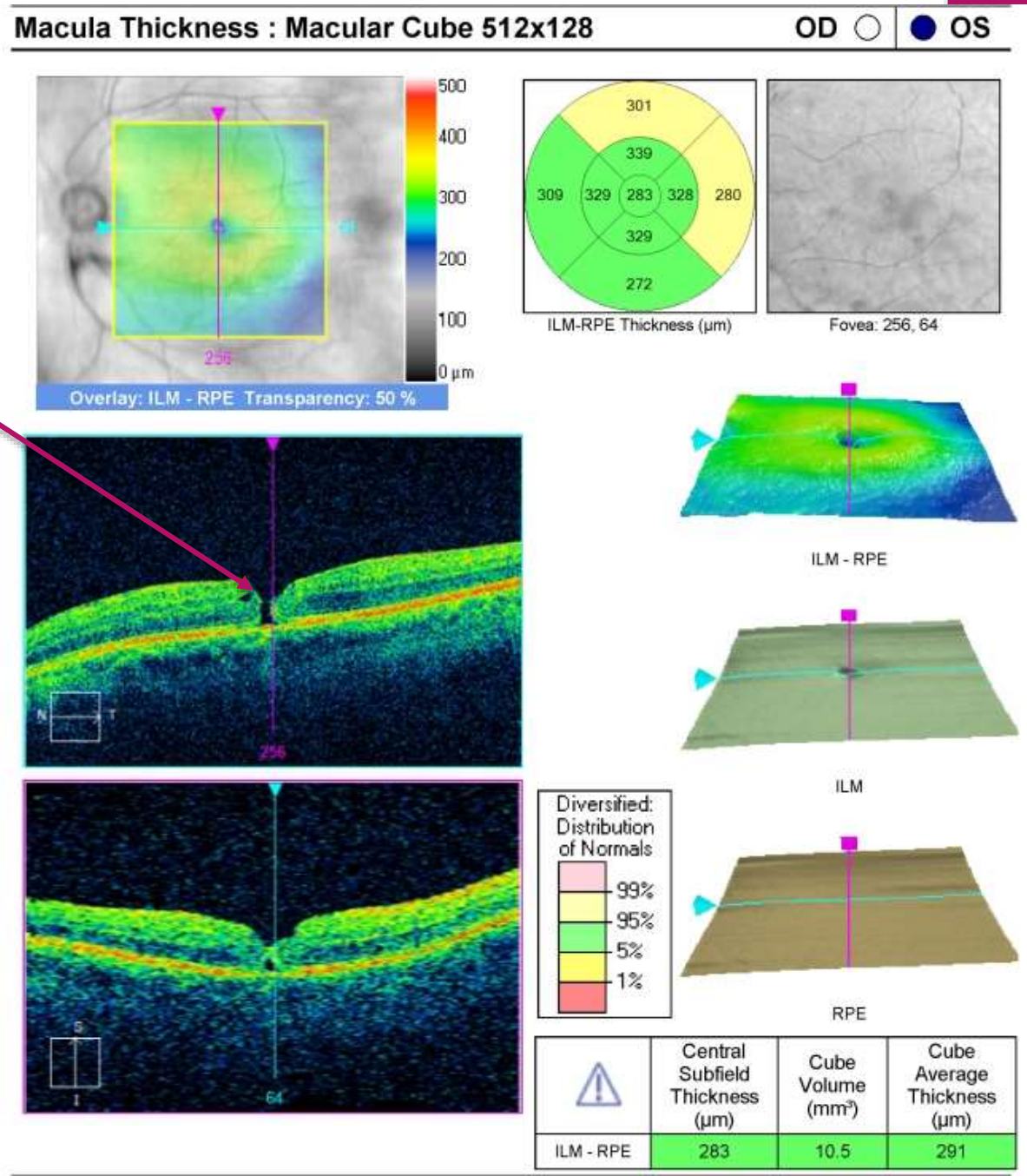
Analyze All B-scans







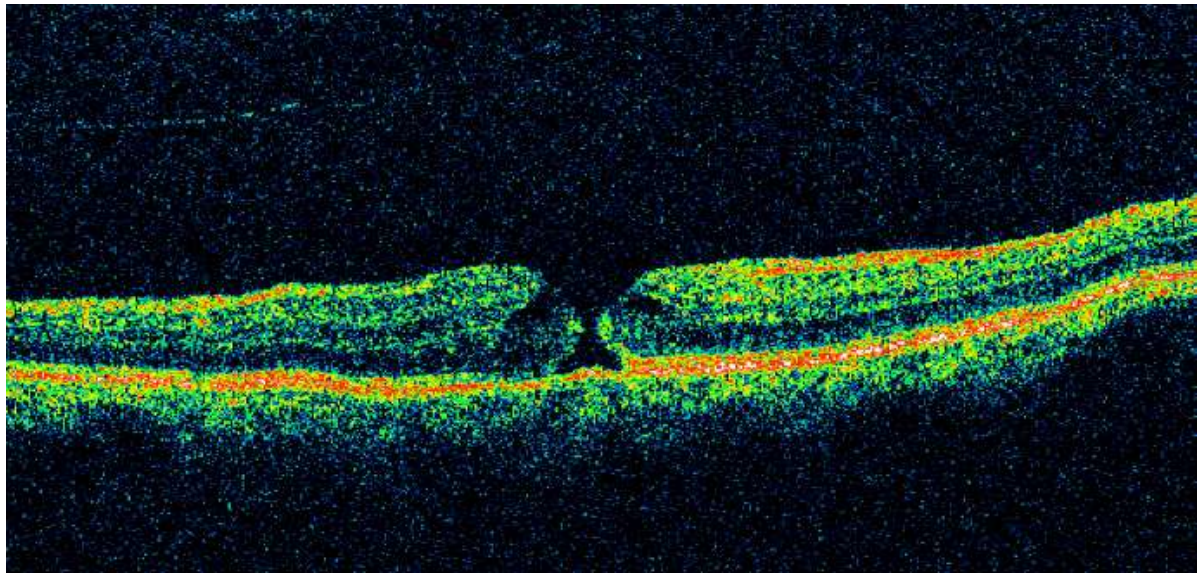
Macular Cube – same patient shows full thickness defect



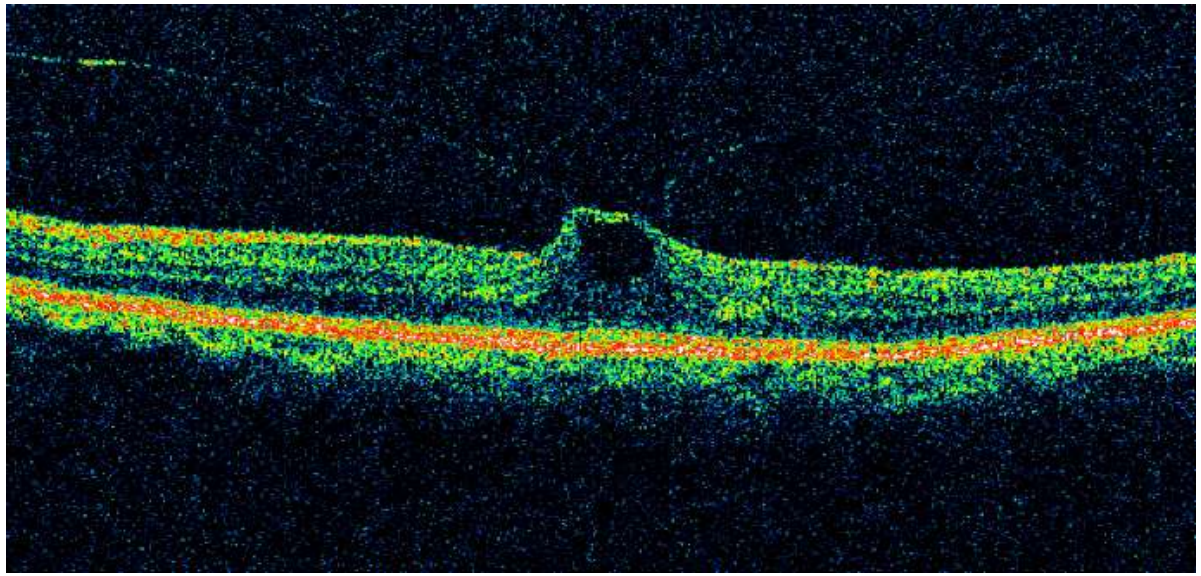
Impending Hole

- Macular hole in one eye
- Contralateral eye has VMT
- Increased risk for development of hole

FTMH OD



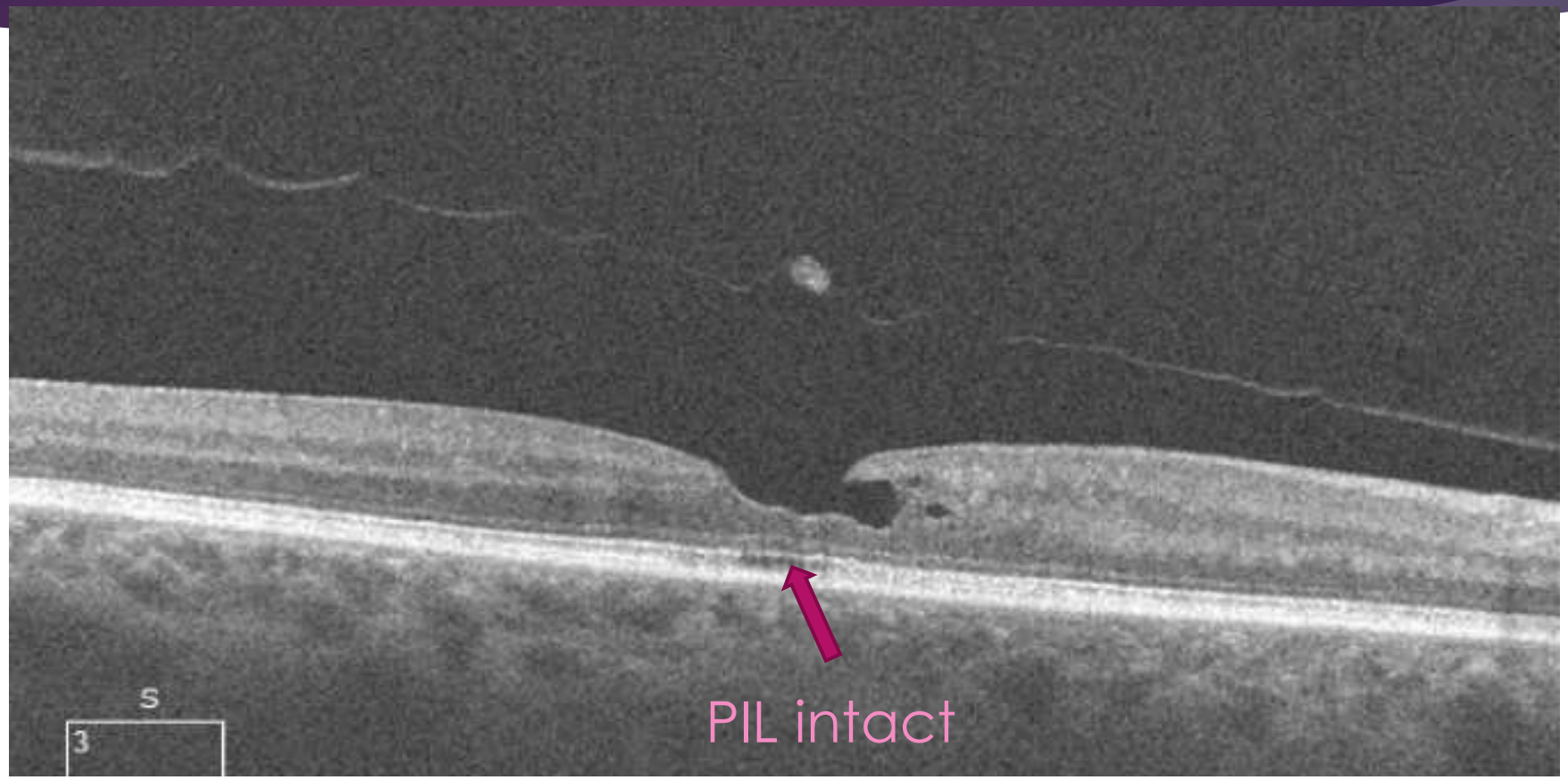
Impending hole (VMT) OS



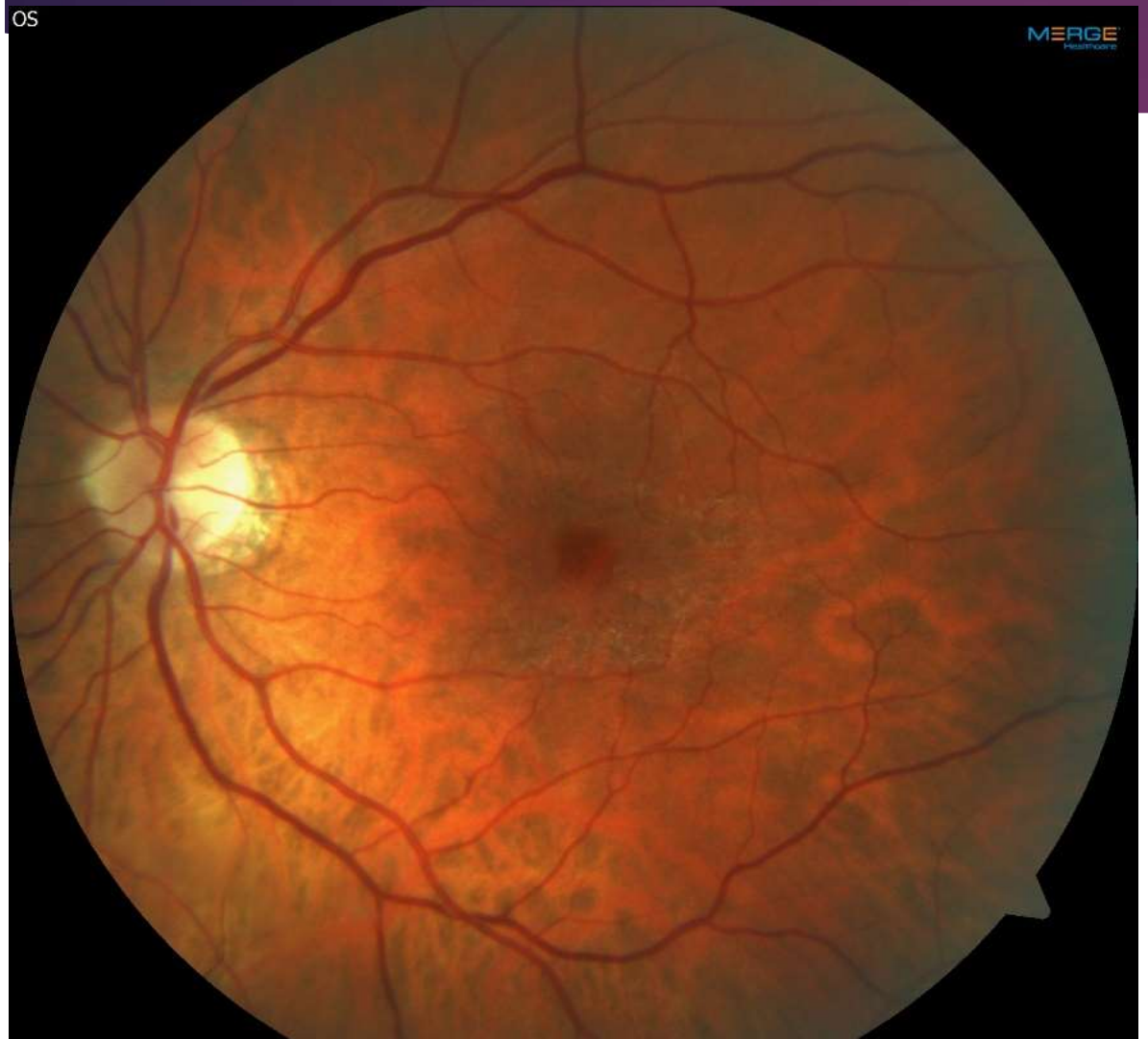
Lamellar Hole

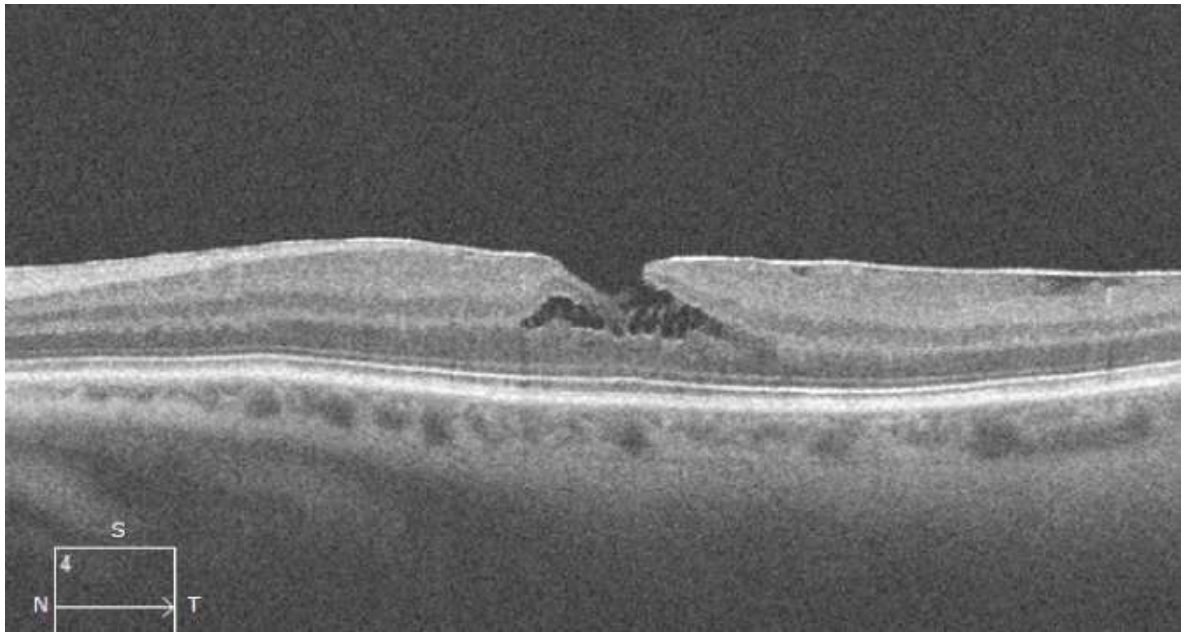
- Partial thickness foveal defect with +/- :
  - Irregular foveal contour
  - Defect in the inner fovea
  - I/R splitting (schisis)
  - * Must have intact photoreceptor layer
- Mechanism: incomplete FTMH formation vs. traction from ERM
- Surgery is controversial; Sxs generally mild

Lamellar Hole



Lamellar Hole from ERM

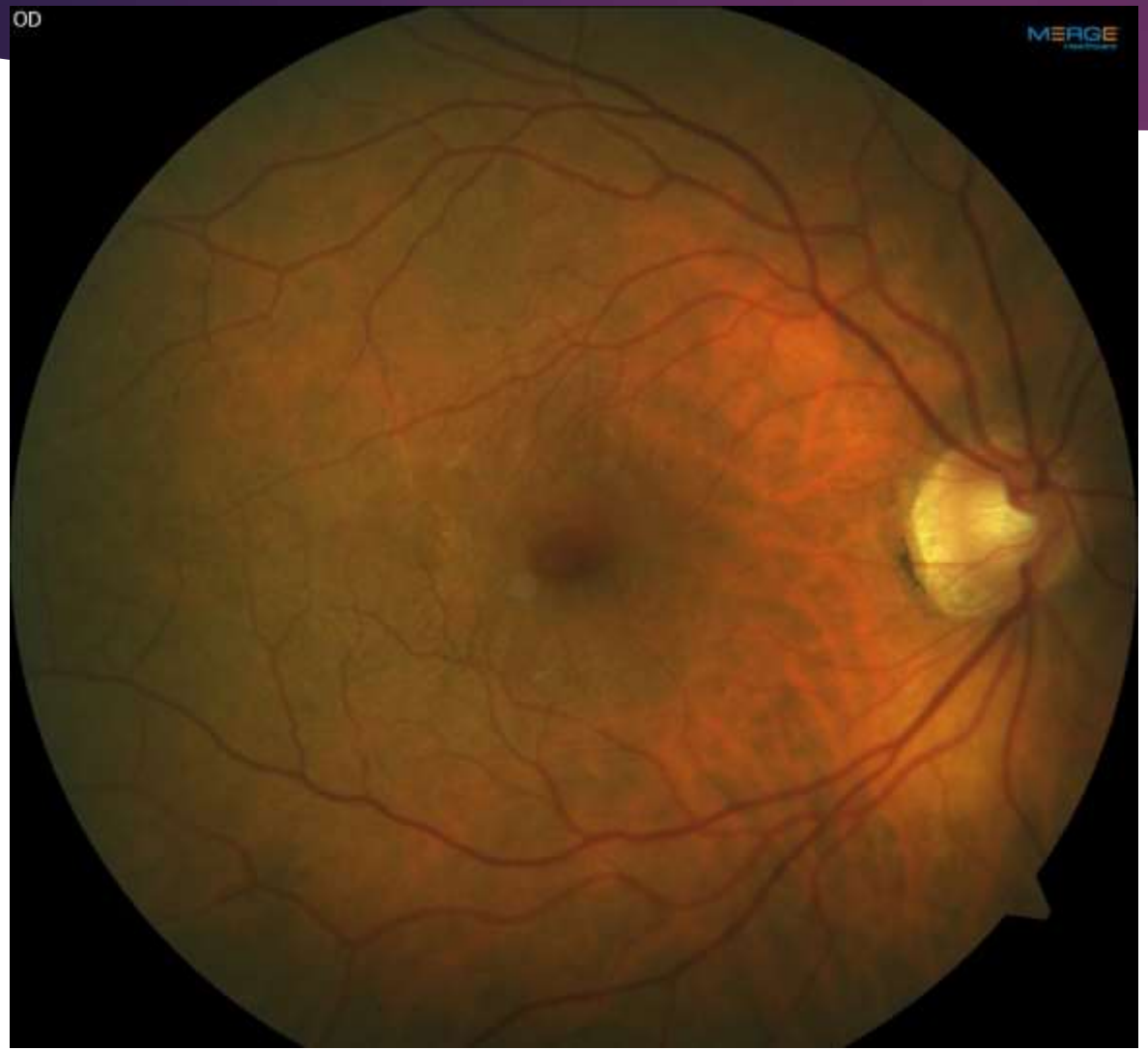


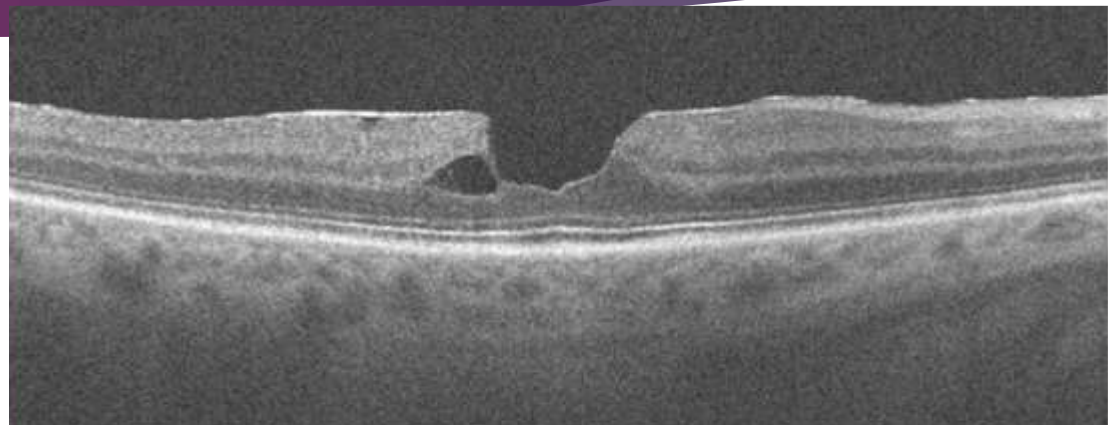


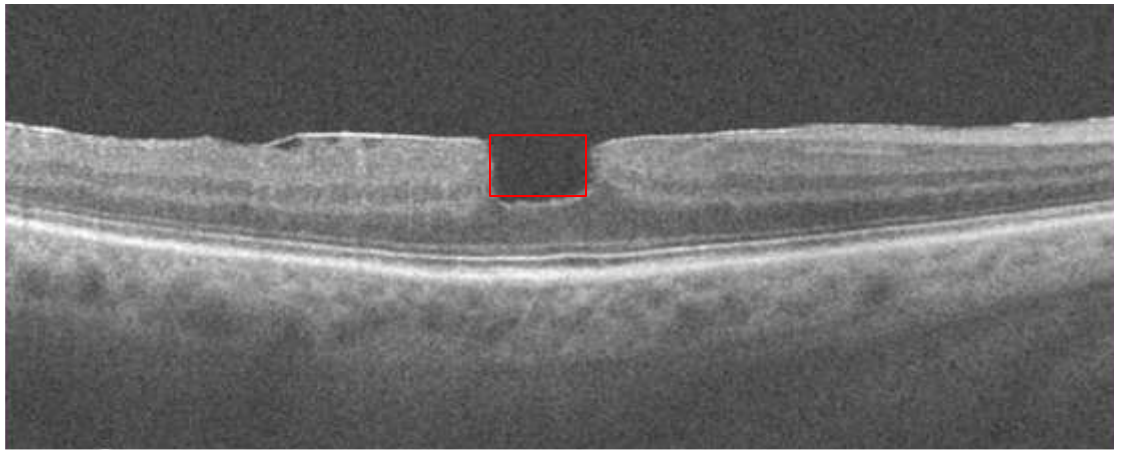
Macular Pseudohole

- Clinical diagnosis only*
- Reddish, round lesion in the fovea on exam -> but no lamellar or FTMH on OCT
- ERM causes pseudohole appearance by distorting the foveal contour
- Squared off shape on OCT

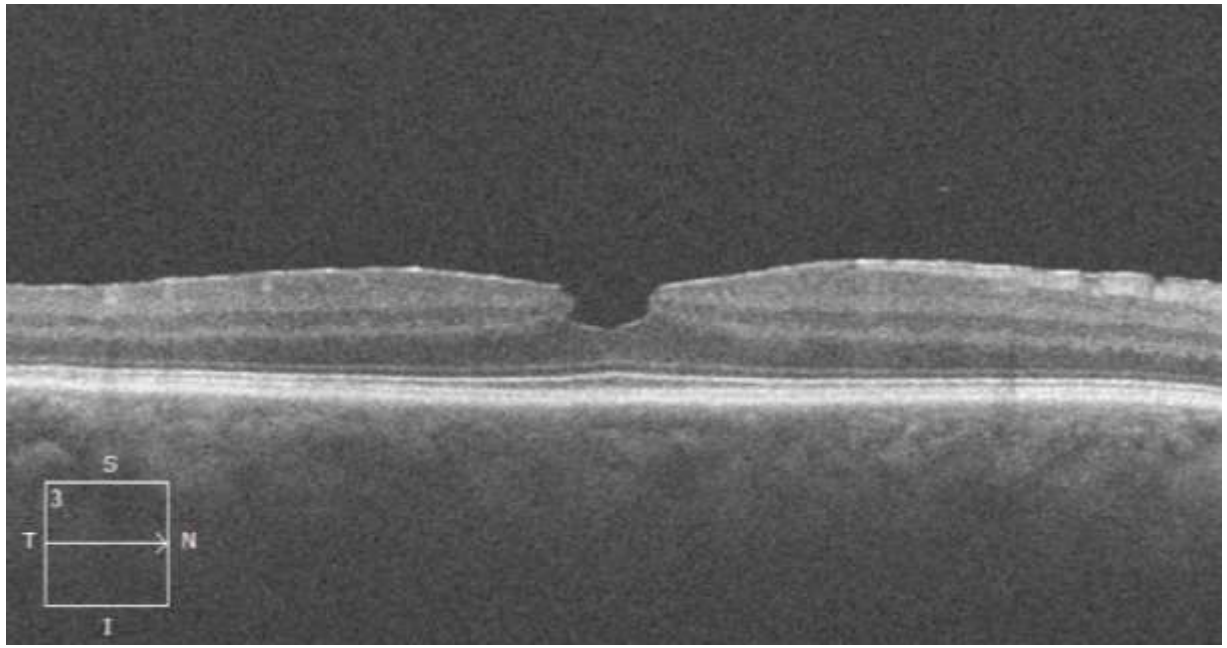
Pseudohole



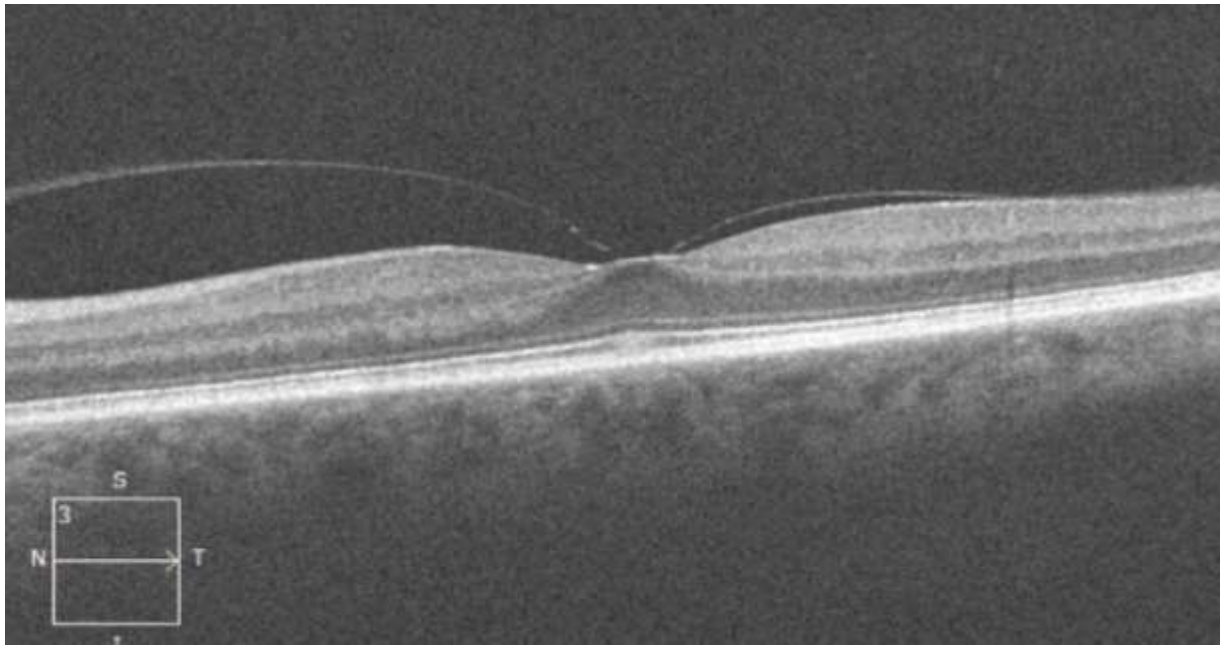




Pseudohole OD



VMT OS



Treatment of VMT and Holes

Jetrea (Ocriplasmin)

- Alpha-2 antiplasmin reducer
- Produces proteolytic activity against protein components within the vitreous body and vitreoretinal interface (laminin, fibronectin, collagen)
- FDA approved in 2012 as treatment for VMT
- Dosage 0.125 mg

Ocriplasmin

- Who are the best candidates for treatment?
  - Under 65
  - No ERM
  - Phakic
  - Focal VMT (vs broad) – the more focal the better
  - Presence of small full thickness hole (>250 microns)
- Only macular holes with concurrent VMT should be considered for ocriplasmin
- At best, ocriplasmin is 50% successful in releasing VMT

Adverse Effects

Floaters

Blurred vision/↓VA

Photopsia - somewhat expected as inducing PVD

Dyschromatopsia

ERG changes

Outer retina OCT changes

Retinal break

Intraocular inflammation

↑IOP

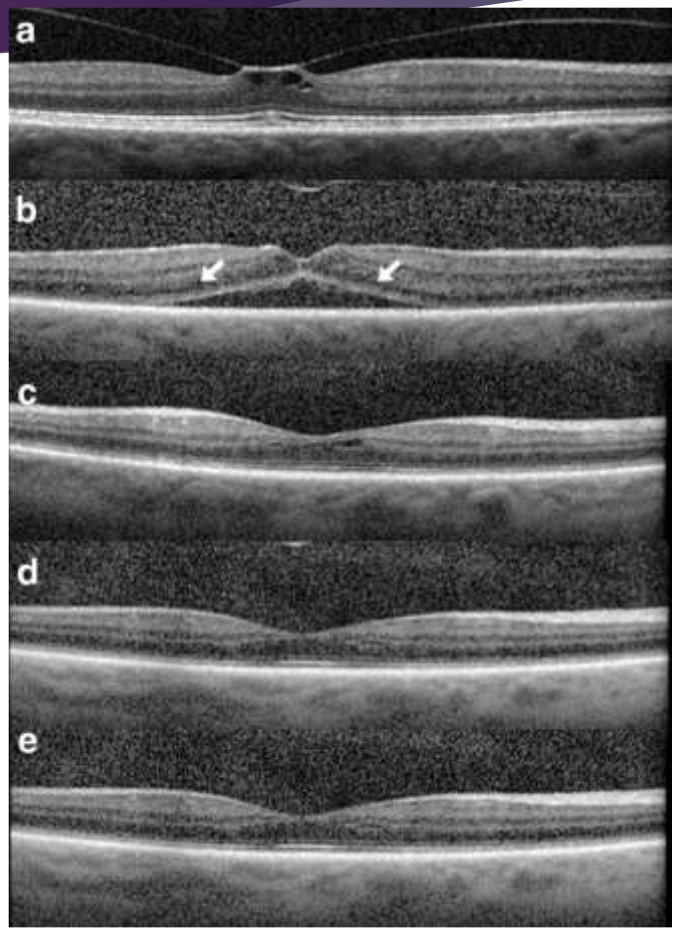
Worsening FTMH

Post-marketing safety concerns were raised over Jetrea - particularly because of outer retinal abnormalities on SD-OCT, ERG changes, and dyschromatopsia

Ocriplasmin

OCT changes post-injection:

- Ellipsoid layer (PIL) disruption
- Accumulation of SRF
  - Correlates with decreased BCVA
  - Generally fully resolve and vision improves
  - Often associated with successful VMT release

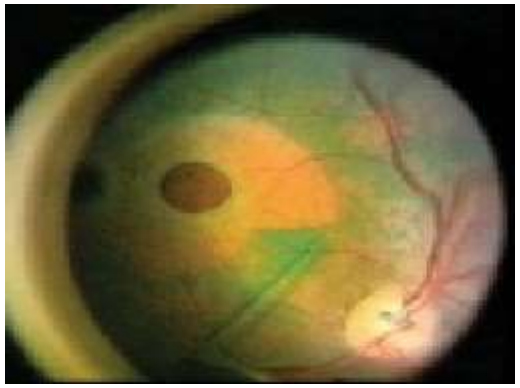


Khan, MA. Ophthalmol Ther 2016

ORBIT

- Ocriplasmin Research to Better Inform Treatment trial
- Simulated “real world” ocriplasmin tx
- 480 patients with symptomatic VMT across 91 sites
- VMT resolution was 45.8% at 1 month, rate of FTMH closure was 30.5% at 1 month
- Adverse drug reactions were reported by 30.6% of patients; 5.2% experienced a serious ADR

Treatment of VMT and Holes



PPV, +/- ILM peel, gas bubble and positioning

- Staining dyes:

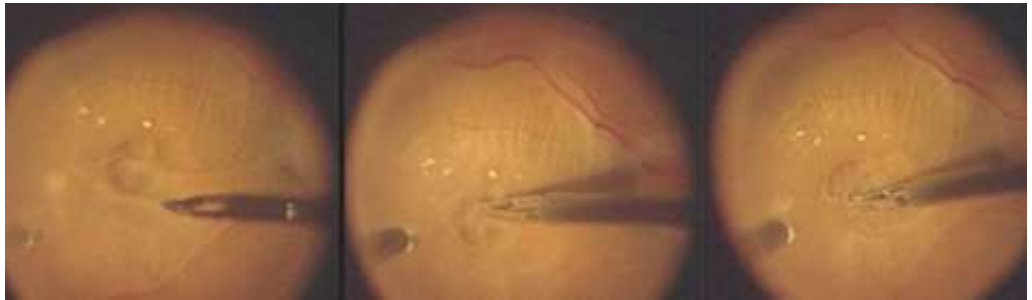
  indocyanine green (ICG)

  trypan blue (TB)*

  brilliant blue G (BBG)* - now FDA approved (TissueBlue™)

  *less toxic

- For larger/chronic macular holes may do an inverted ILM flap or ILM patch



Inverted ILM flap
Lai, Retina Today

Face Down Positioning?

- Face down positioning -> traditional standard of care
  - 5 days to 1 week after surgery for idiopathic macular hole repair
- Trending now toward minimal face down time or even none at all
  - Equally successful in closure rates and end BCVA
  - Still have to keep at 45˚ degrees for the first days and sleep on side
  - Great news for patients!

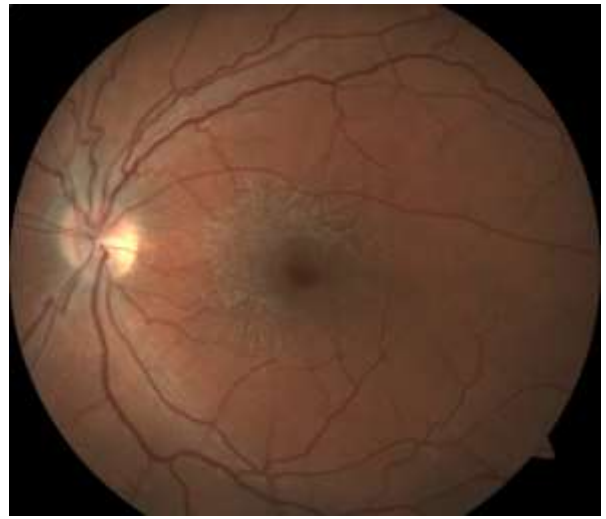
Alternative Treatment

Pneumatic vitreolysis

- Induction of PVD via 0.3 mL 100% C_3F_8 gas or 0.3 mL of 100% SF_6
- Lower cost vs ocriplasmin or PPV
- Small studies have shown high success rates (better than ocriplasmin), but still need more data

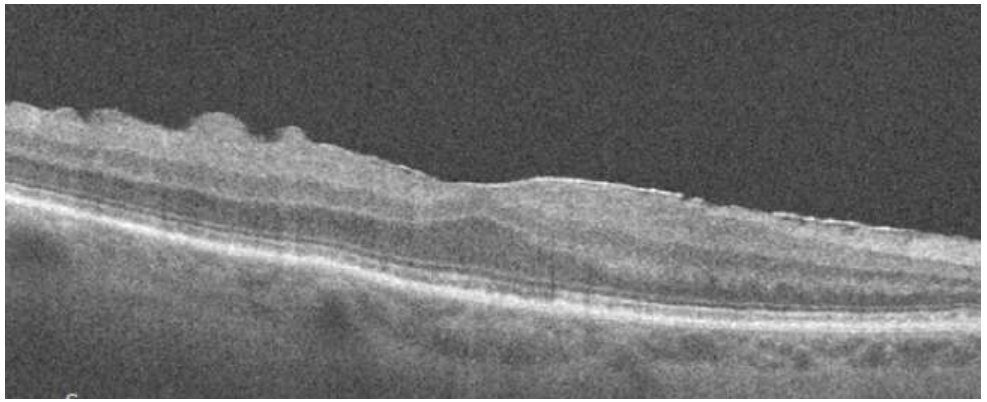
Epiretinal Membrane (ERM)

- AKA: macular pucker, cellophane maculopathy
- Fibrocellular proliferation found at the vitreoretinal interface made of up vitreous cortex remnants and glial cells
- Generally occurs after PVD
- Can cause macular traction which then can result in anatomical changes
- Occurs idiopathically or 2/2 proliferative retinopathies, inflammatory conditions, trauma, hx of RD

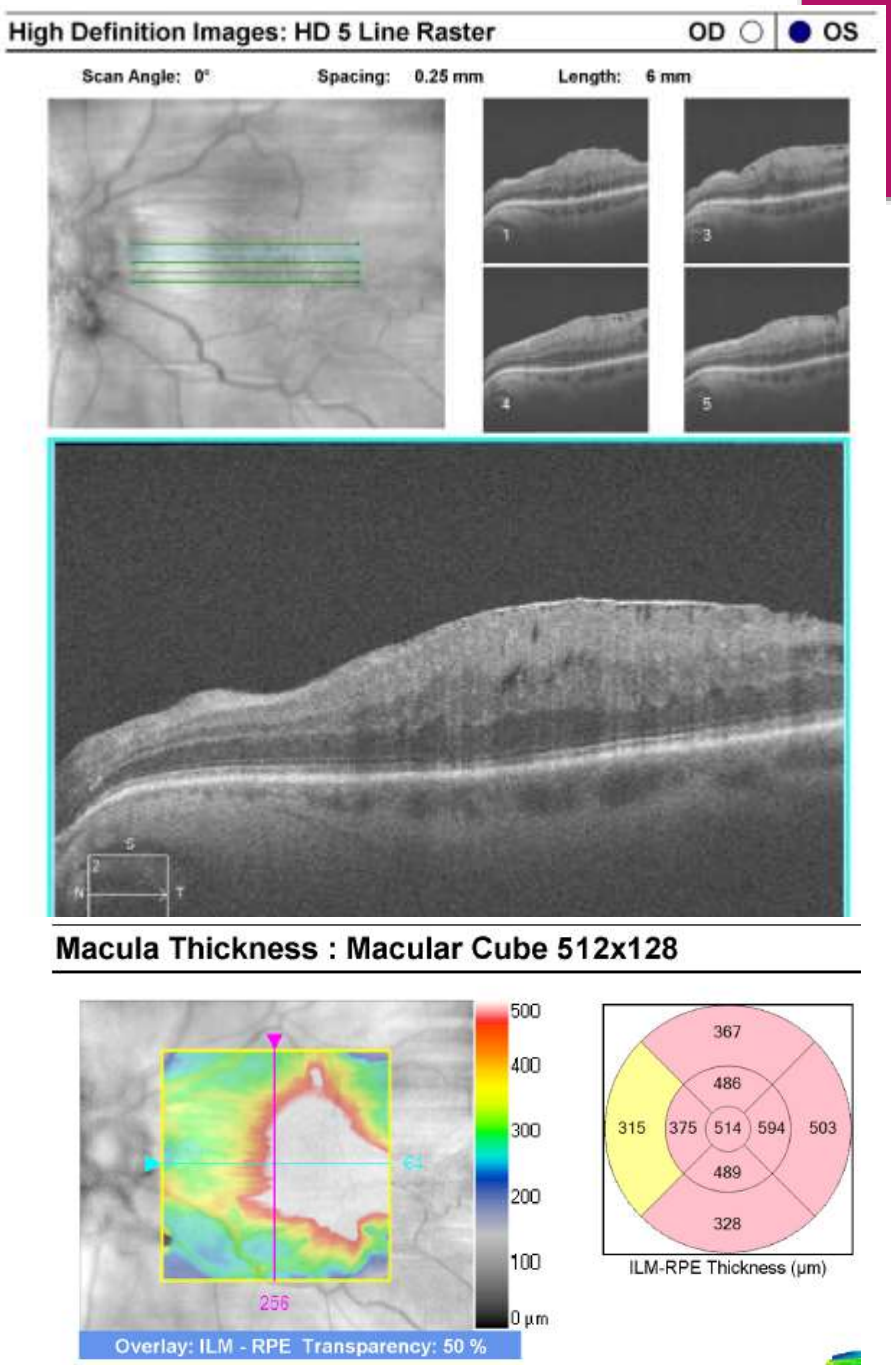


ERM

- Prevalence increases with age (>60)
  - peak prevalence observed in 8th decade (11.6-35.7%)
- Sxs (if present): decreased VA, metamorphopsia, and central photopsia
- Surgical Tx: vitrectomy with ILM peel




OS
MERGE


High Definition Images: HD 5 Line Raster
OD
OS
Scan Angle: 0°
Spacing: 0.25 mm
Length: 6 mm
1
3
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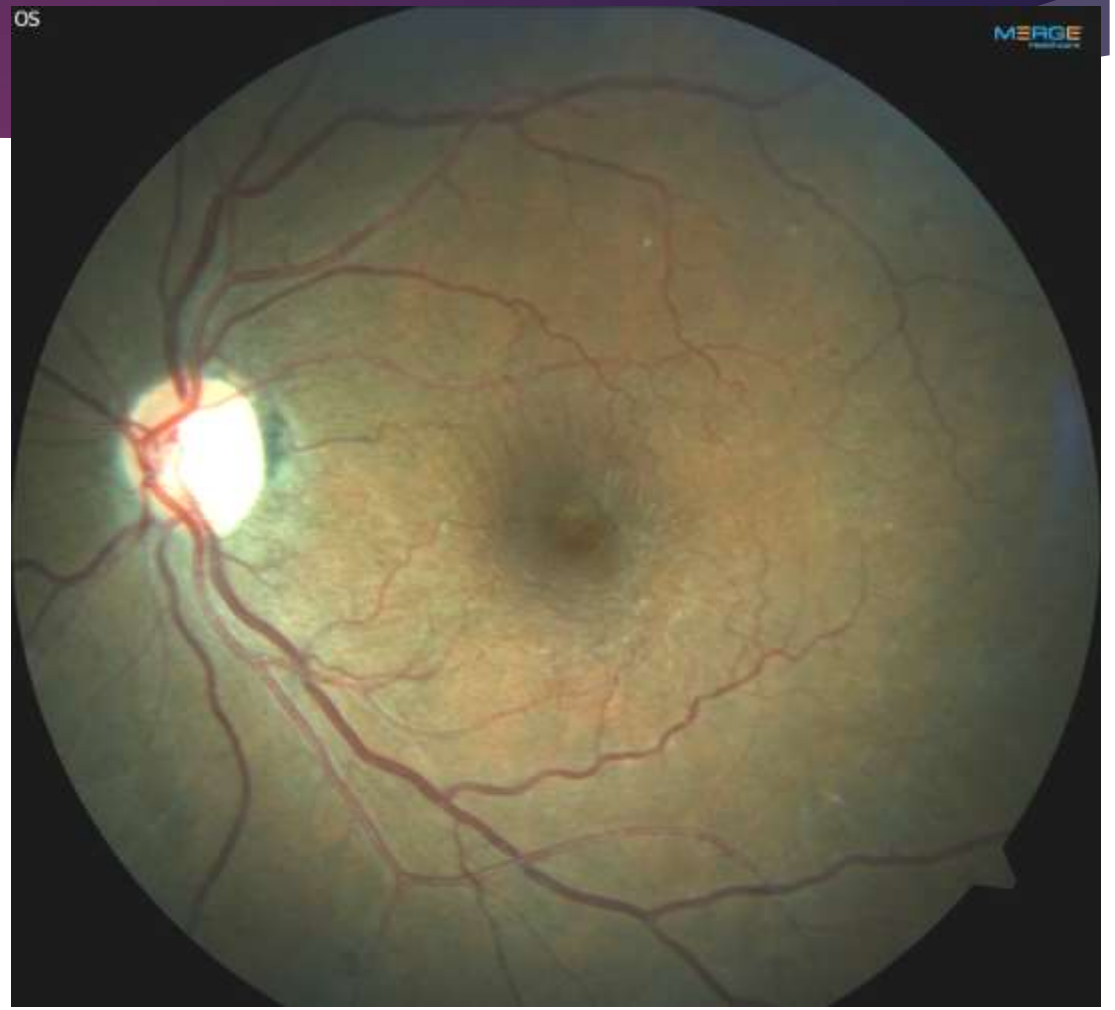
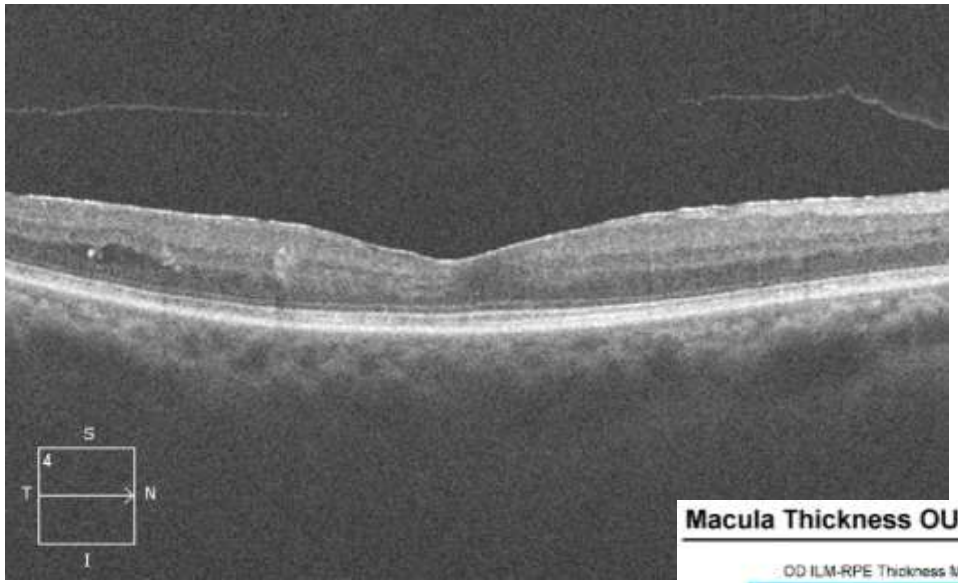
T
Macula Thickness : Macular Cube 512x128
500
400
300
200
100
0 µm
256
367
486
315
375
514
594
503
489
328
ILM-RPE Thickness (µm)
Overlay: ILM - RPE Transparency: 50 %

ERM with DR

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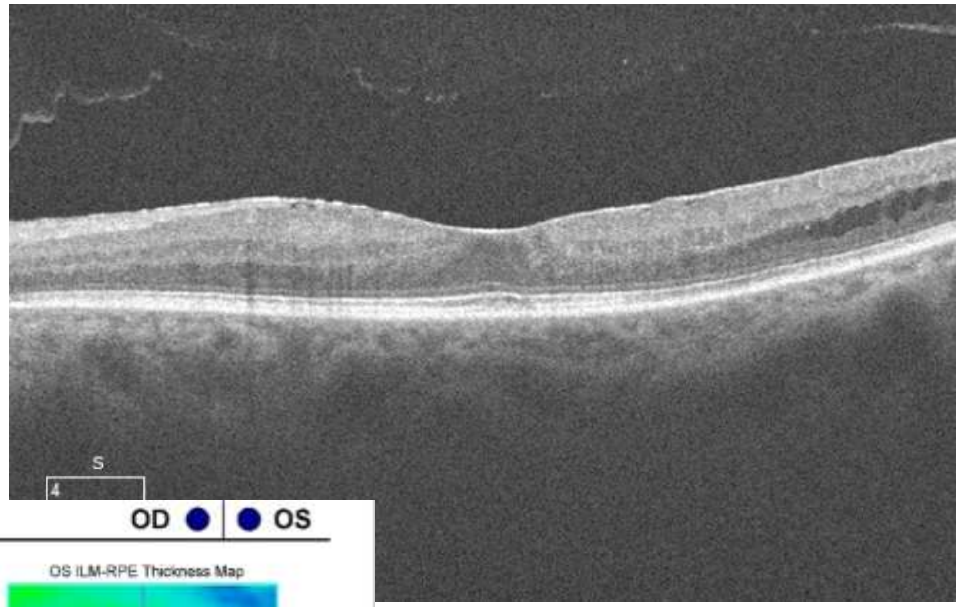
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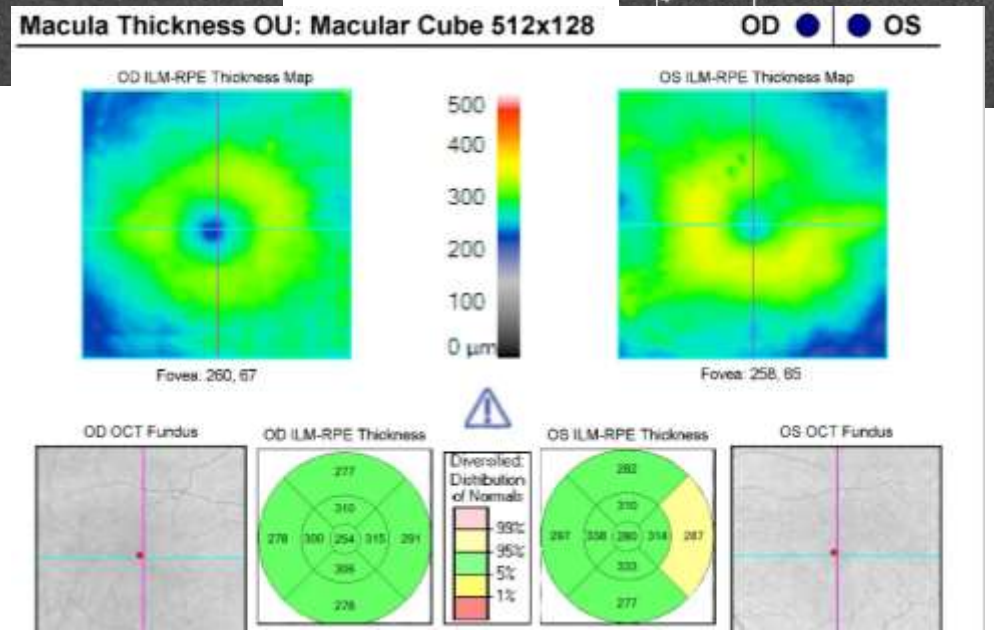
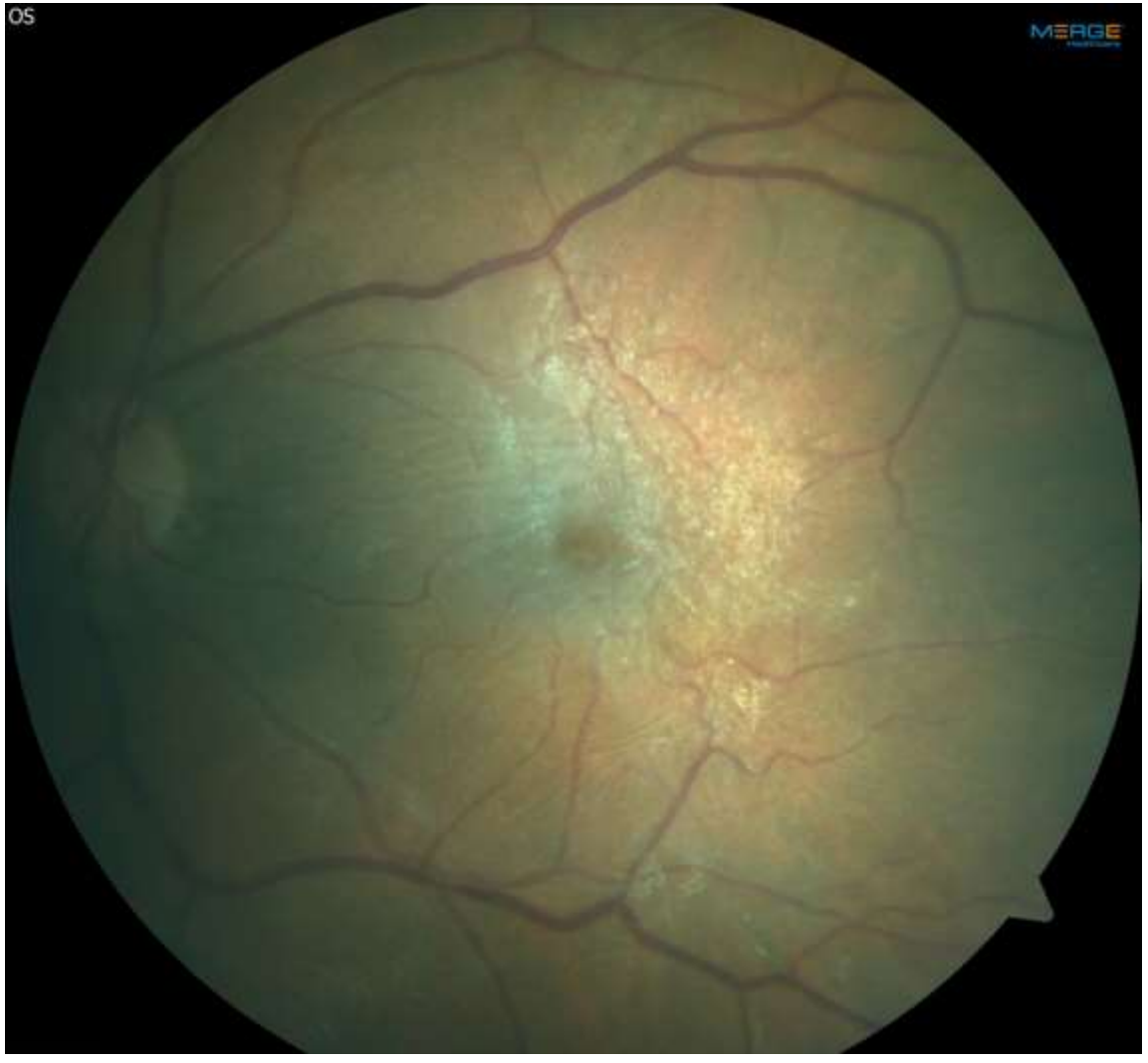
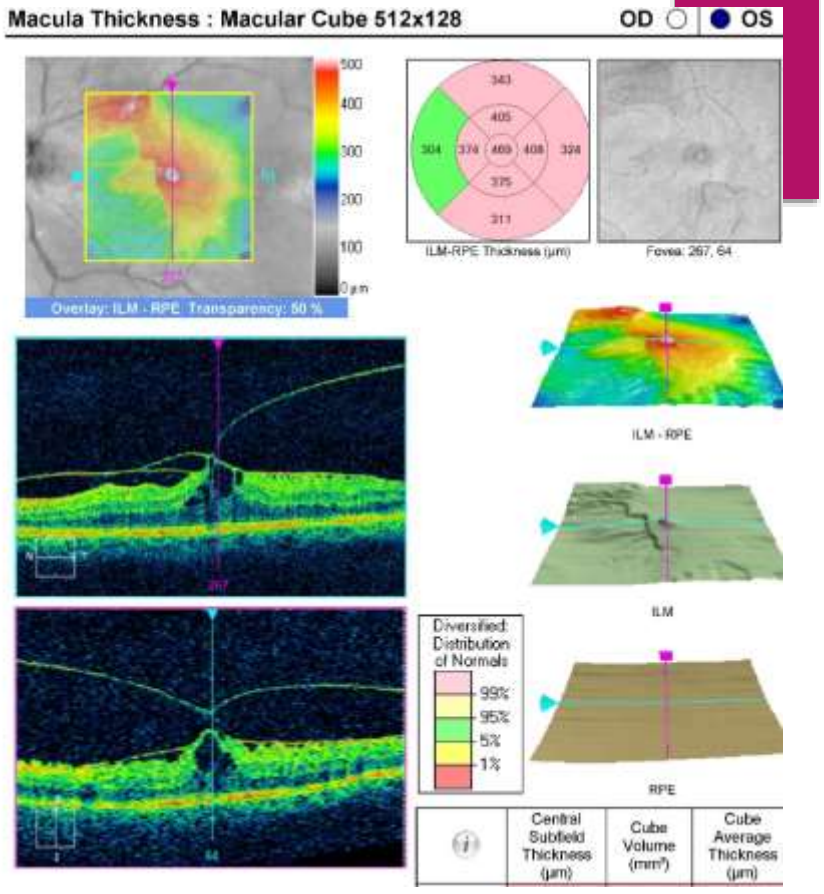
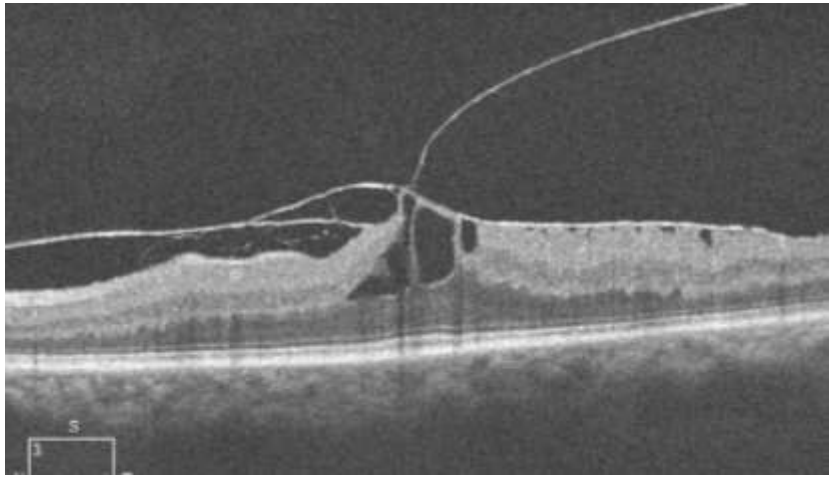

Macula Thickness OU: Macular Cube 512x128
OD
OS
OD ILM-RPE Thickness Map
OS ILM-RPE Thickness Map
500
400
300
200
100
0 µm
Fovea: 260, 67
Fovea: 258, 85
OD OCT Fundus
OD ILM-RPE Thickness
Diversified Distribution of Normals
99%
95%
5%
1%
OS ILM-RPE Thickness
OS OCT Fundus


OS
MERGE


Macula Thickness : Macular Cube 512x128
OD
OS
500
400
300
200
100
0 µm
343
405
304
374
469
408
324
375
311
ILM-RPE Thickness (µm)
Fovea: 267, 64
Overlay: ILM - RPE, Transparency: 50 %
ILM - RPE
ILM
Diversified Distribution of Normals
99%
95%
5%
1%
RPE
Central Subfield Thickness (µm)
Cube Volume (mm³)
Cube Average Thickness (µm)



Surgery

PPV, ERM peel (+/- ILM peel)

- VA recovery at 2-3 months after ERM peeling, though can be 6-12 months before reaching BCVA
- Better prognosis for recovery when idiopathic
- Risk of ERM recurrence w/o simultaneous ILM peel

Take Home

- PVD process takes many years to develop
- Anomalous PVD can cause complication at many sites in the eye including the macula
- OCT imaging allows for better classification of the vitreomacular interface following the IVTS Classification System
  - VMA
  - VMT
  - FTMH (small, medium or large)