Managing the Vitreomacular Interface
A Guide to VMA, VMT, Holes and ERM

Anna K. Bedwell, OD, FAAO, FORS
Clinical Associate Professor
Indiana University School of Optometry
**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
Responsible for defining VMI disorders

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

Jay S. Duker, MD, Peter K. Kaiser, MD, Suzanne Binder, MD, Marc D. de Smet, MD, Alain Gaudric, MD, Elias Rekhter, MD, Steinhoff R. Sudda, MD, Jerry Sebag, MD, Richard F. Spaide, MD, Peter Stalmans, MD, PhD

Objective: The International Vitreomacular Traction Study 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.

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 © 2013 by the American Academy of Ophthalmology.
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 posterior hyaloid vitreous cortex Focal
PREVALENCE OF VITREOMACULAR ADHESION IN PATIENTS WITHOUT MACULOPATHY OLDER THAN 40 YEARS

JULIE A. RODMAN, OD, MS,* DIANA SHECHTMAN, OD,* BRAD M. SUTTON, OD,†
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
Vitreomacular Traction (VMT)

- Partial detachment of the vitreous in the perifoveal area with corresponding retinal abnormality
  - (i.e.: 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
d

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 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

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

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

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

285 microns
FTMH – large/chronic

488 microns
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
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

PIL intact
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
• 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
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
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$_3$F$_8$ 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 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 8\textsuperscript{th} decade (11.6-35.7%)
- Sxs (if present): decreased VA, metamorphopsia, and central photopsia
- Surgical Tx: vitrectomy with ILM peel
ERM with DR
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
• 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)