

Intravitreal Injections in AMD: When to Stop Treating Your Patient

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AMD is the third leading cause of blindness globally.

The burden is as **3.7 million** patients will be living with AMD by 2030.

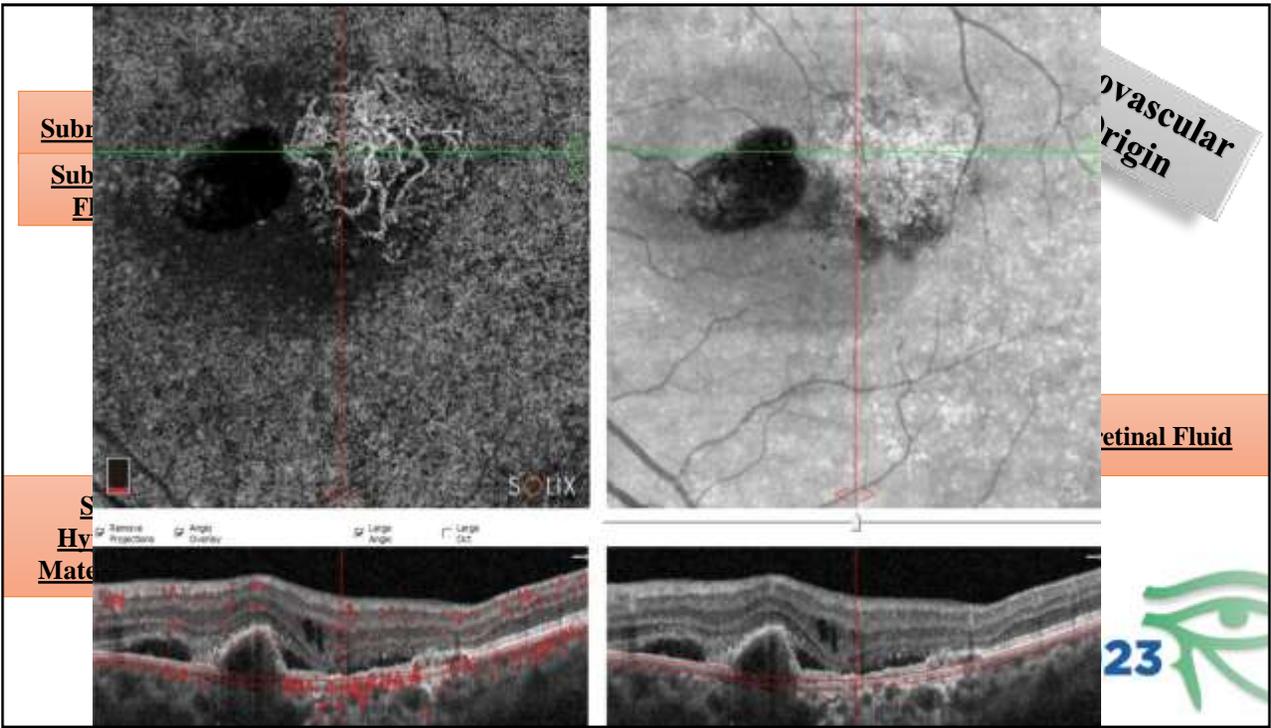
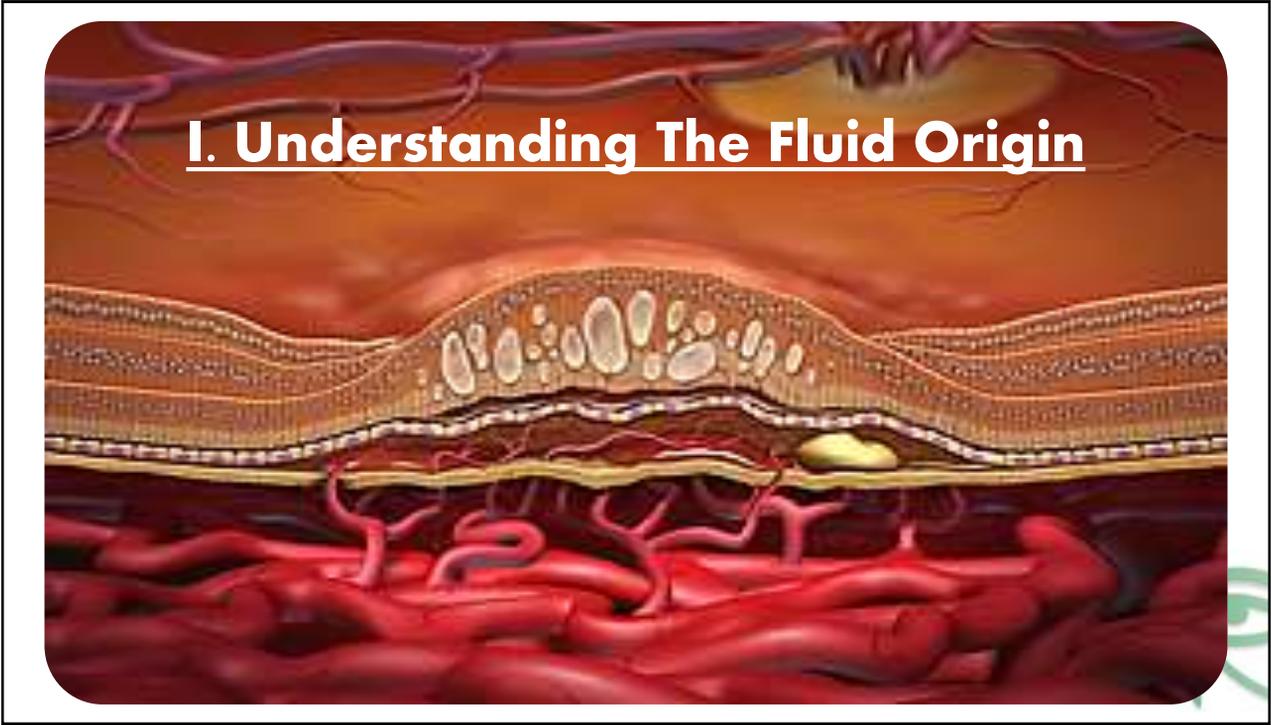


- Intravitreal injections of anti VEGF is the current mainstay treatment for neovascular AMD.
- Retreatment decisions are largely based on OCT biomarkers of neovascular activity (IRF, SRF, SHRM).



- However, recommendations regarding optimal OCT anatomic **endpoints** are lacking.
- Although achieving a fluid-free macula formed the basis of fixed dosing regimens trials (Bevacizumab, Ranibizumab, Aflibercept).
- Some degree of persistent fluid is common, as was seen in nearly half of the eyes receiving monthly injections of ranibizumab in the Comparisons of AMD Treatment Trials (CATT) at the end of 2 years.







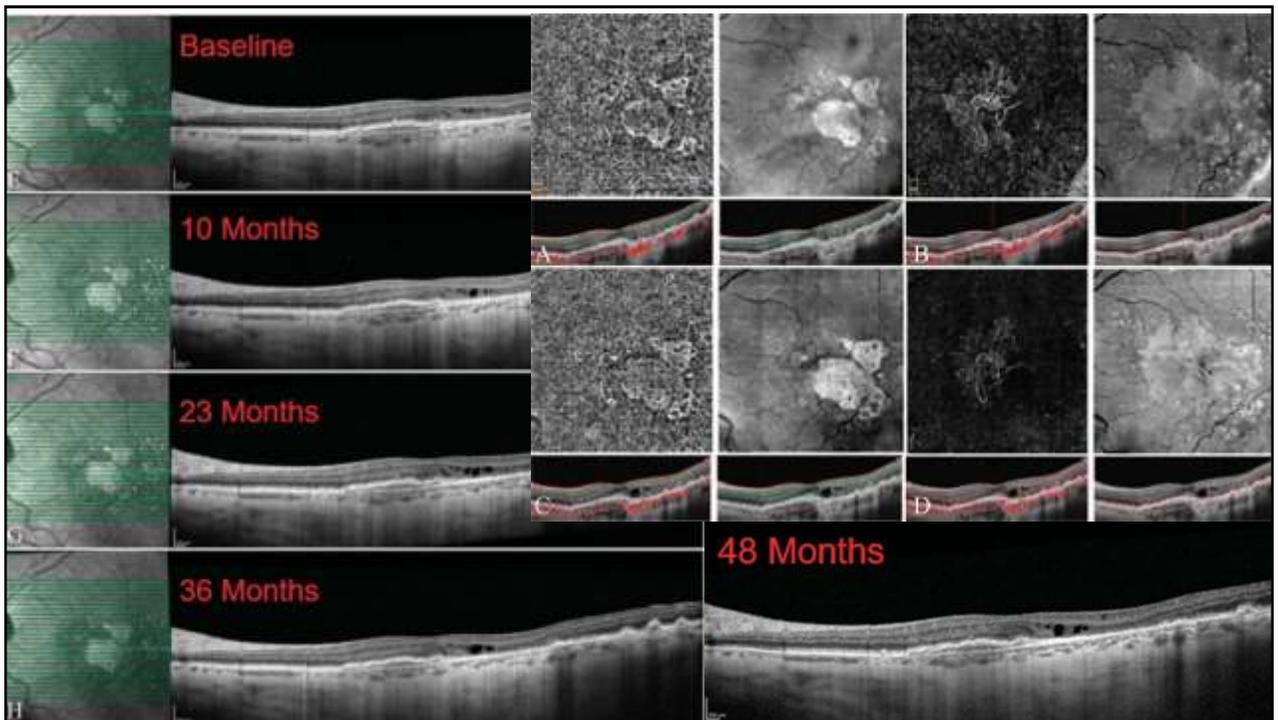


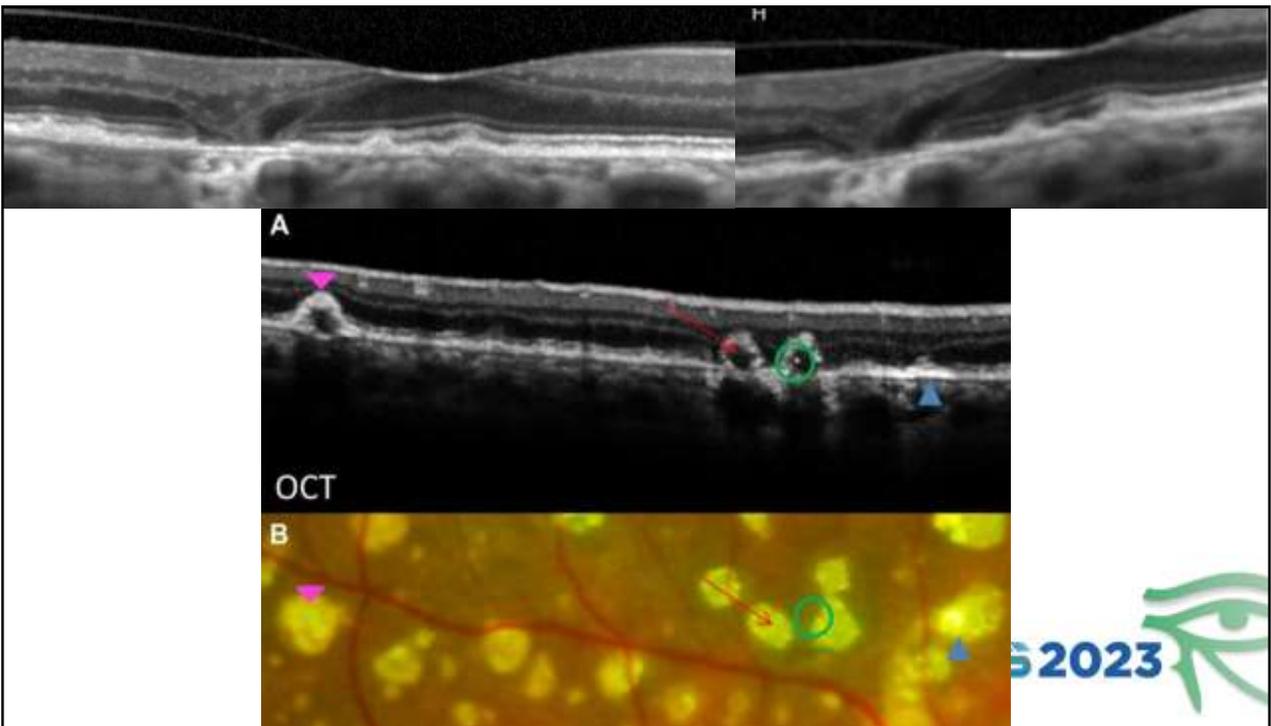
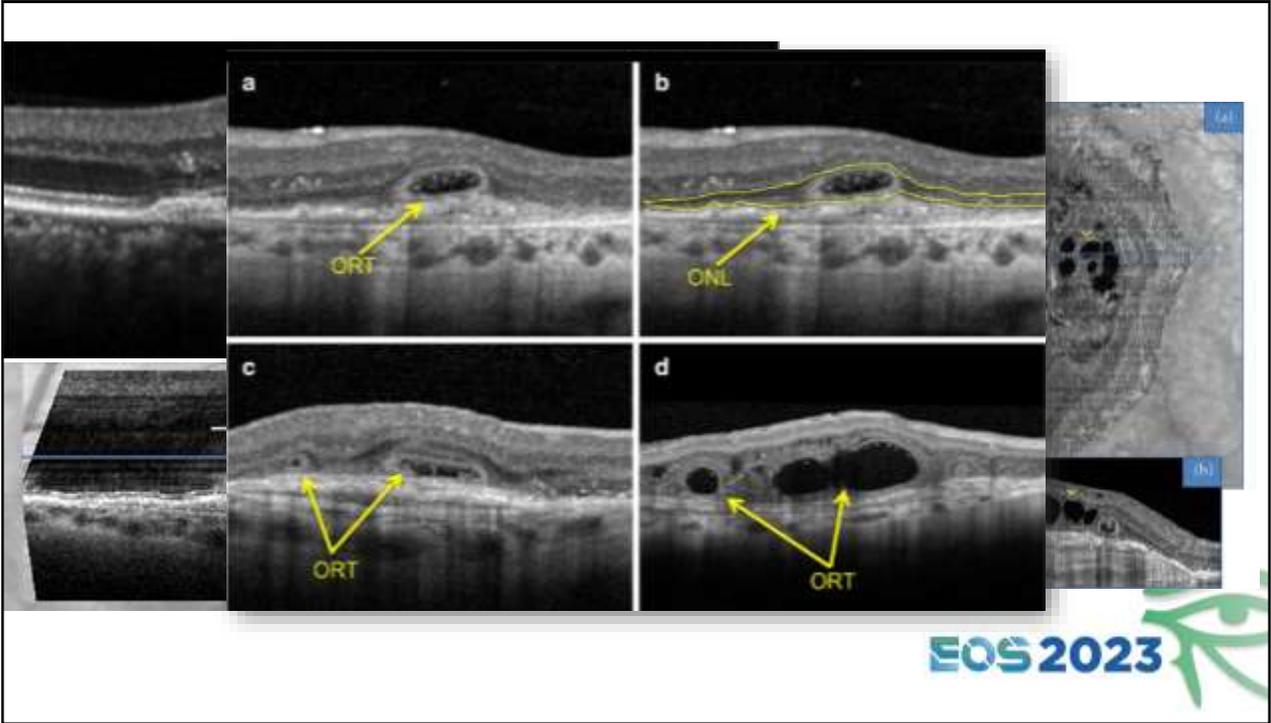
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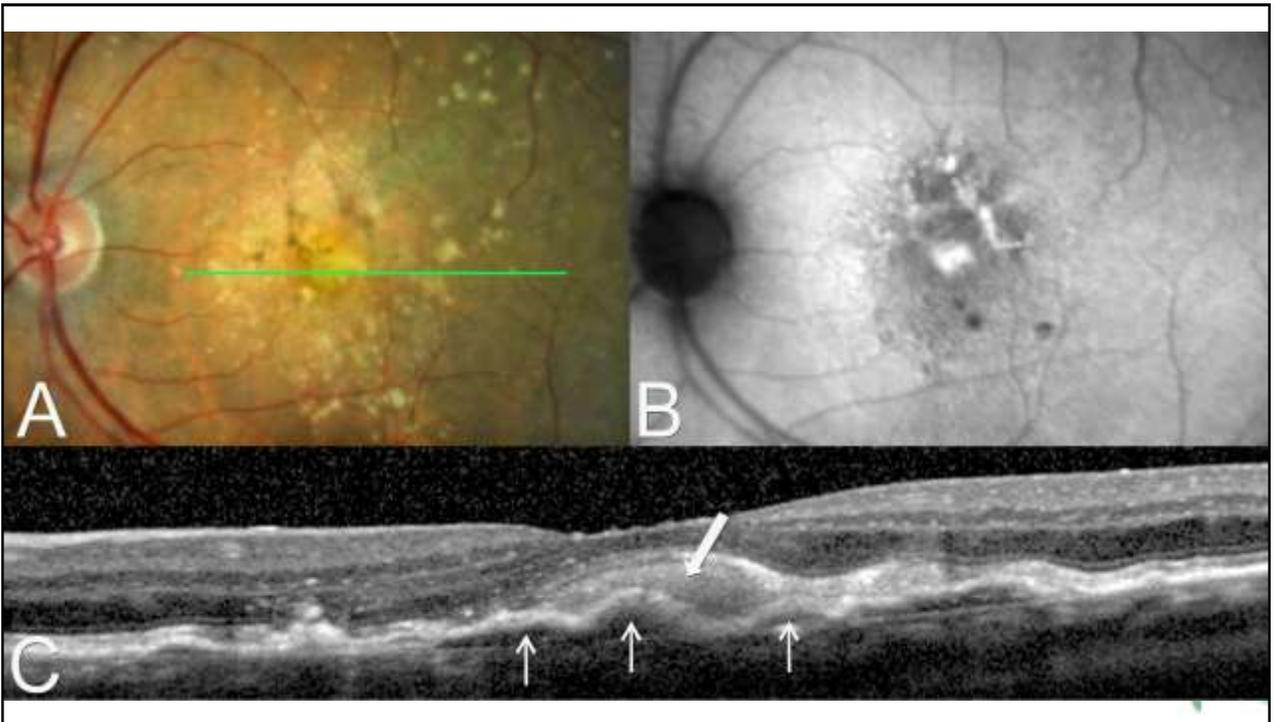
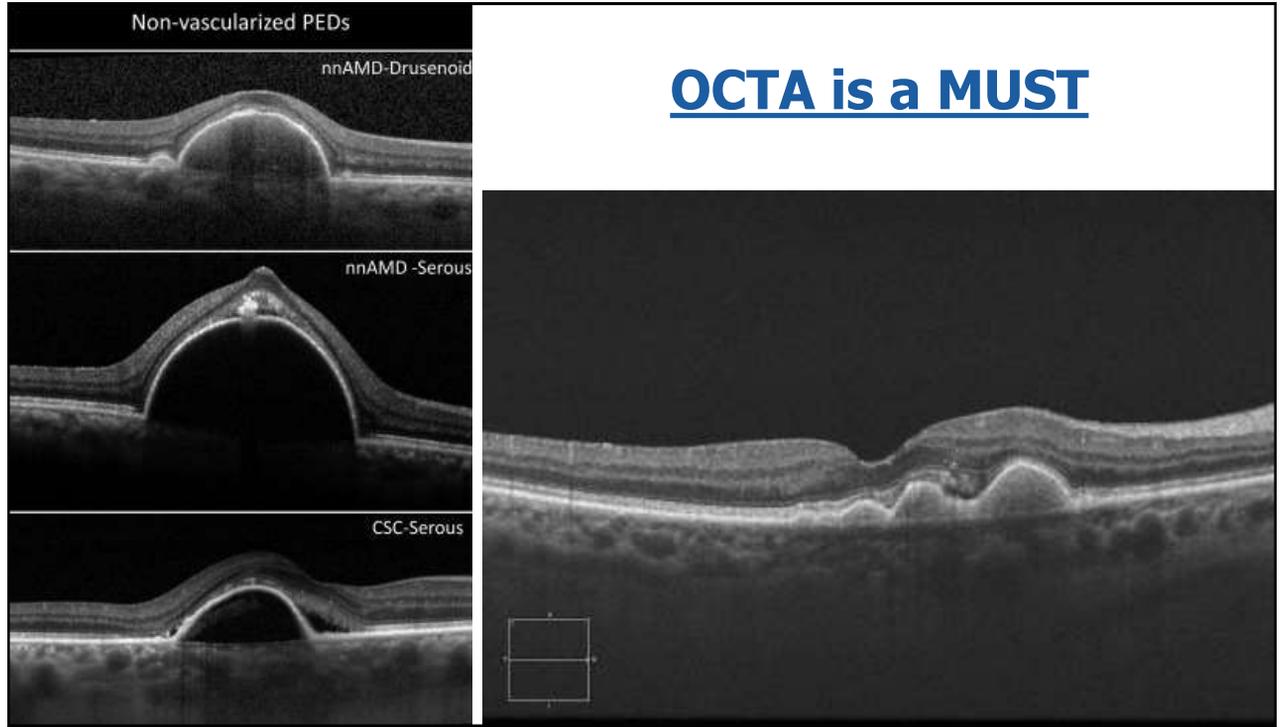
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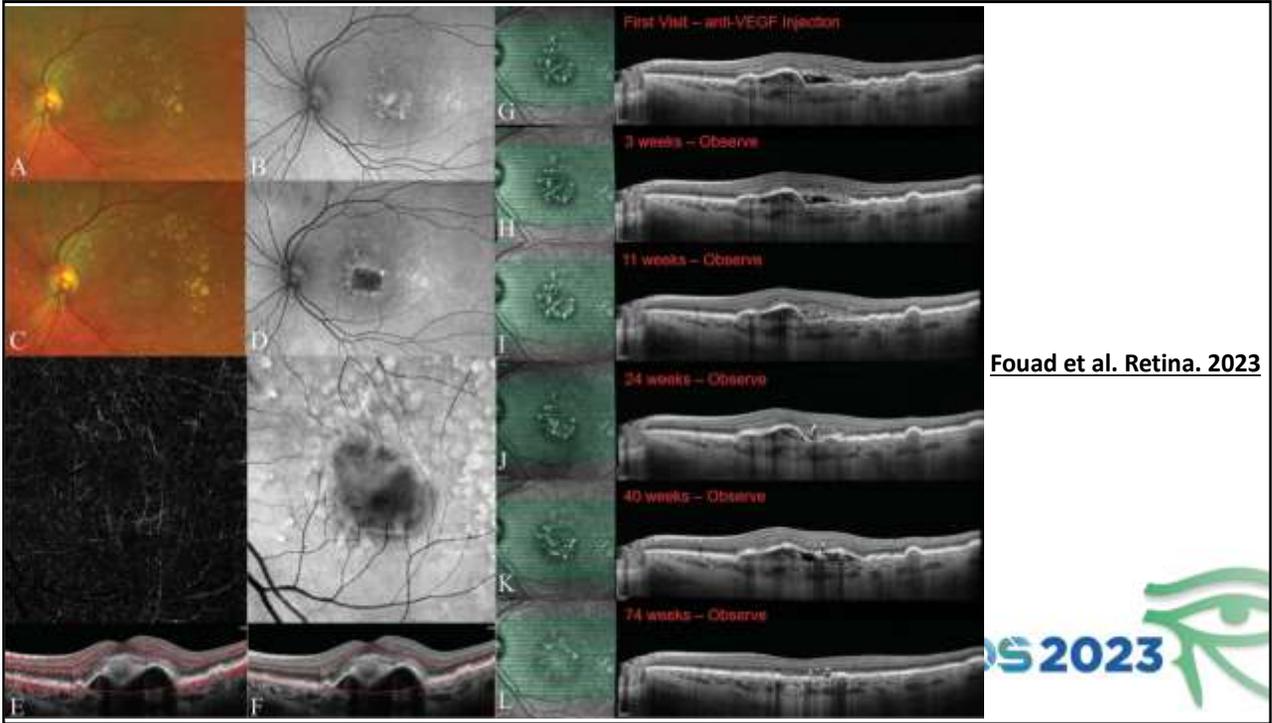
Pathways of Fluid Leakage in Age Related Macular Degeneration

Fouad, Yousef A. MD^{1,2}; Santina, Ahmad MD¹; Bousquet, Elodie MD, PhD^{1,3}; Sadda, Srinivas R. MD⁴; Sarraf, David MD¹

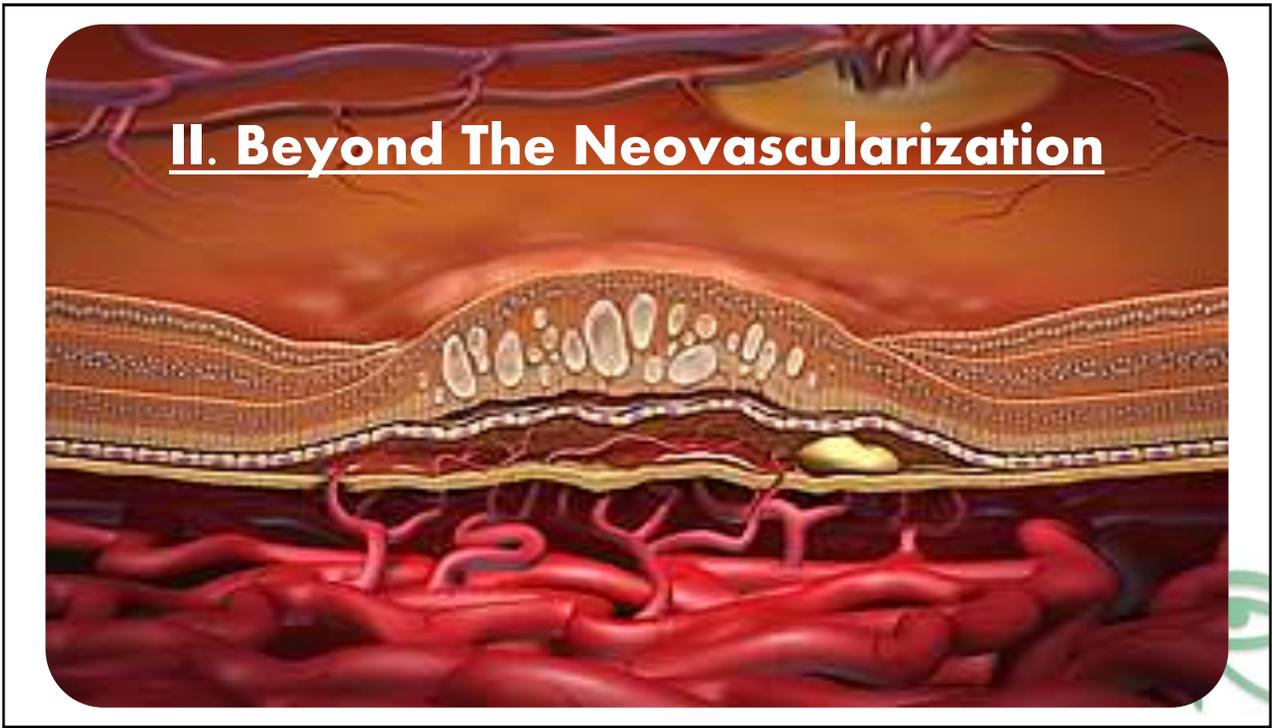




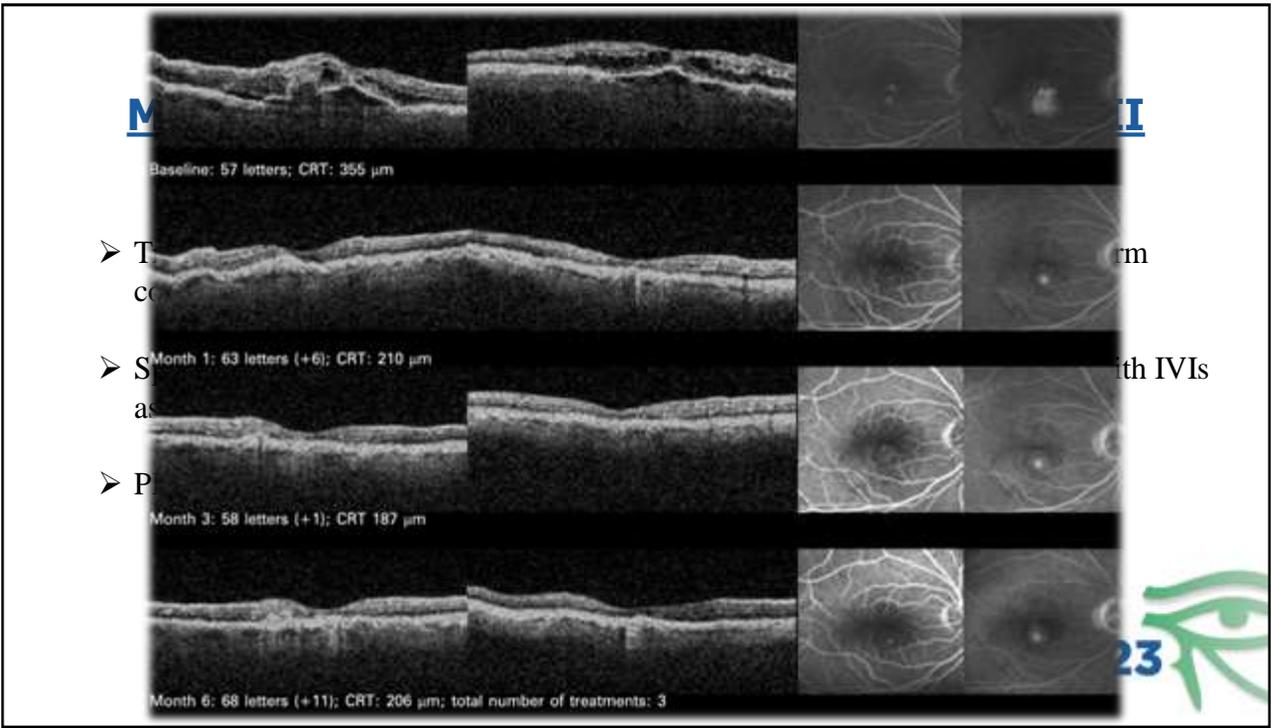
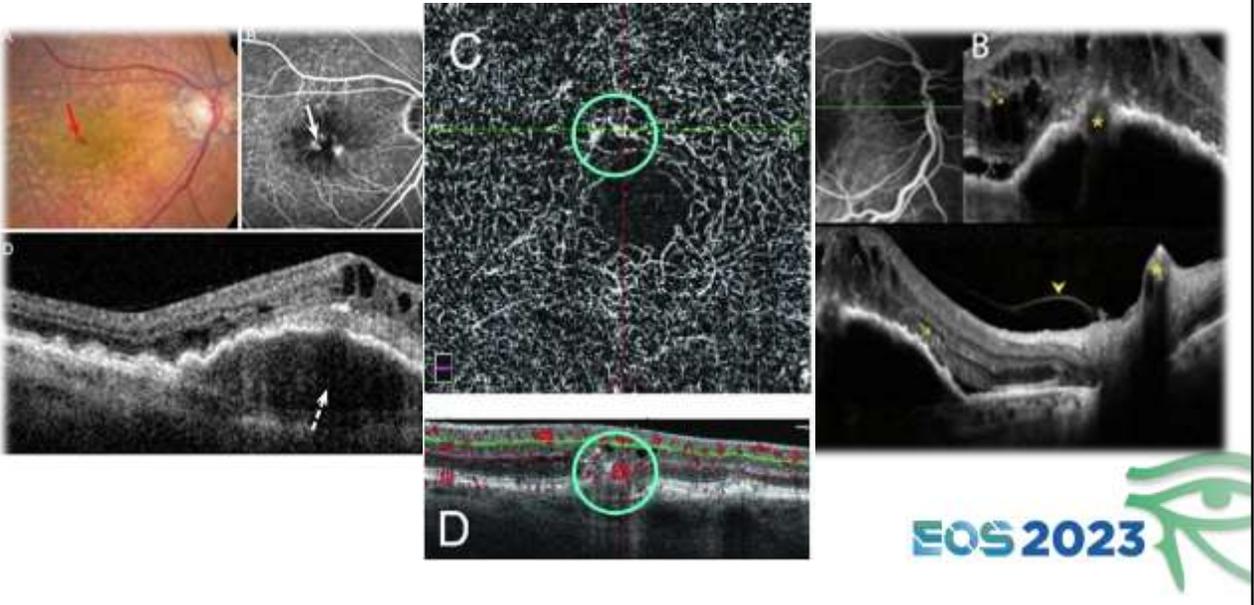


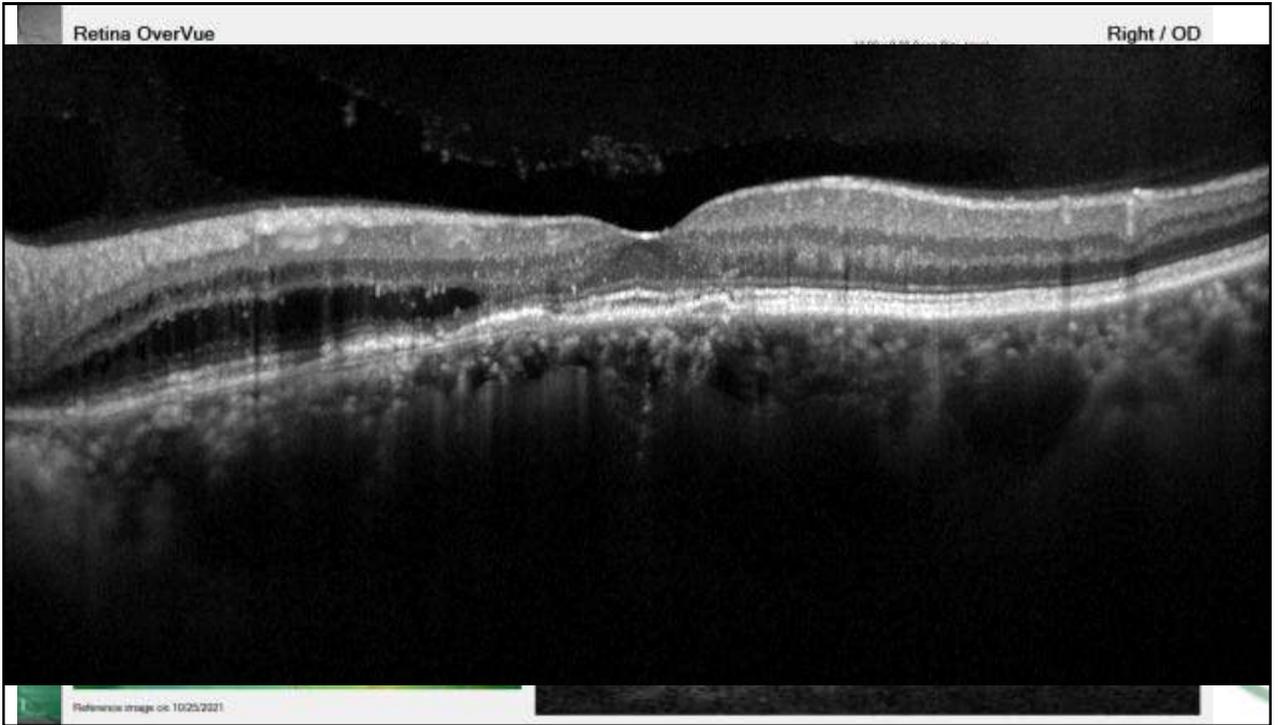


Fouad et al. Retina. 2023



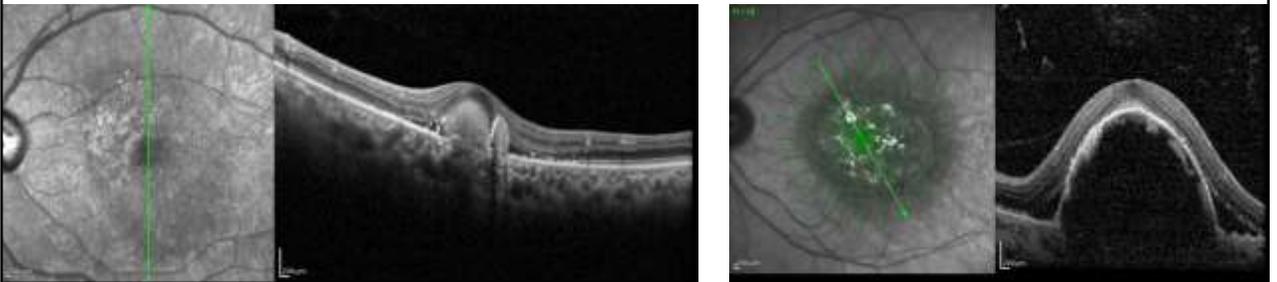
Macular Neovascular Membrane (MVN) Type III



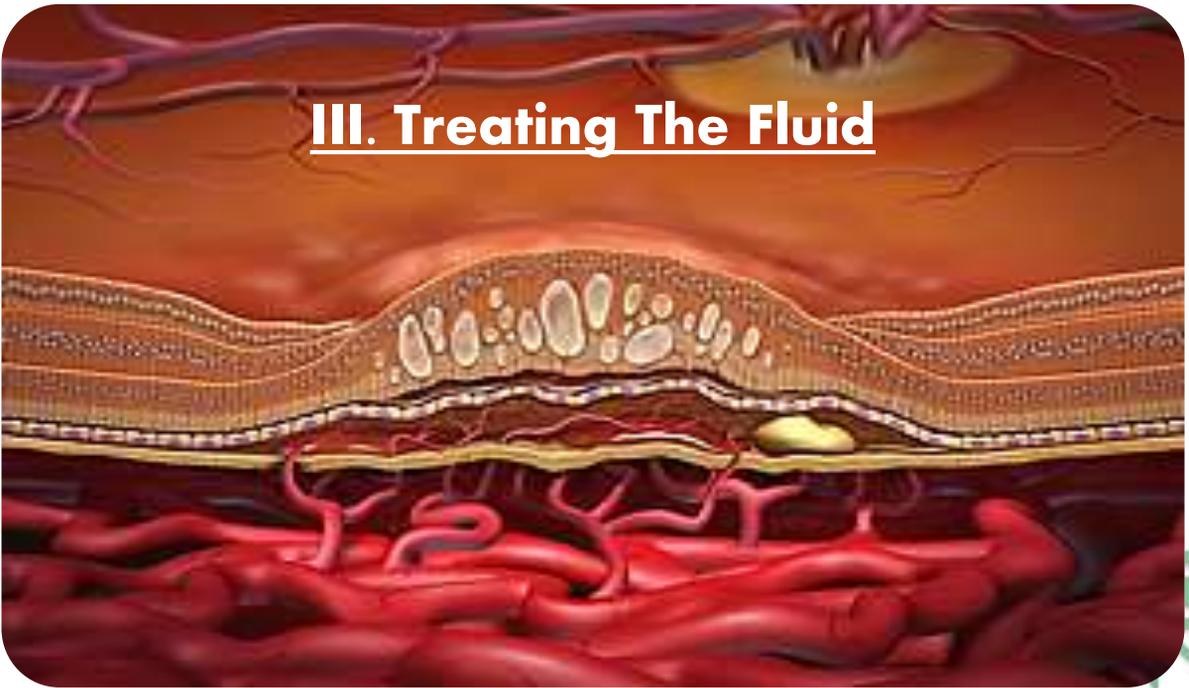


Polypoidal Choroidal Vasculopathy (PCV)

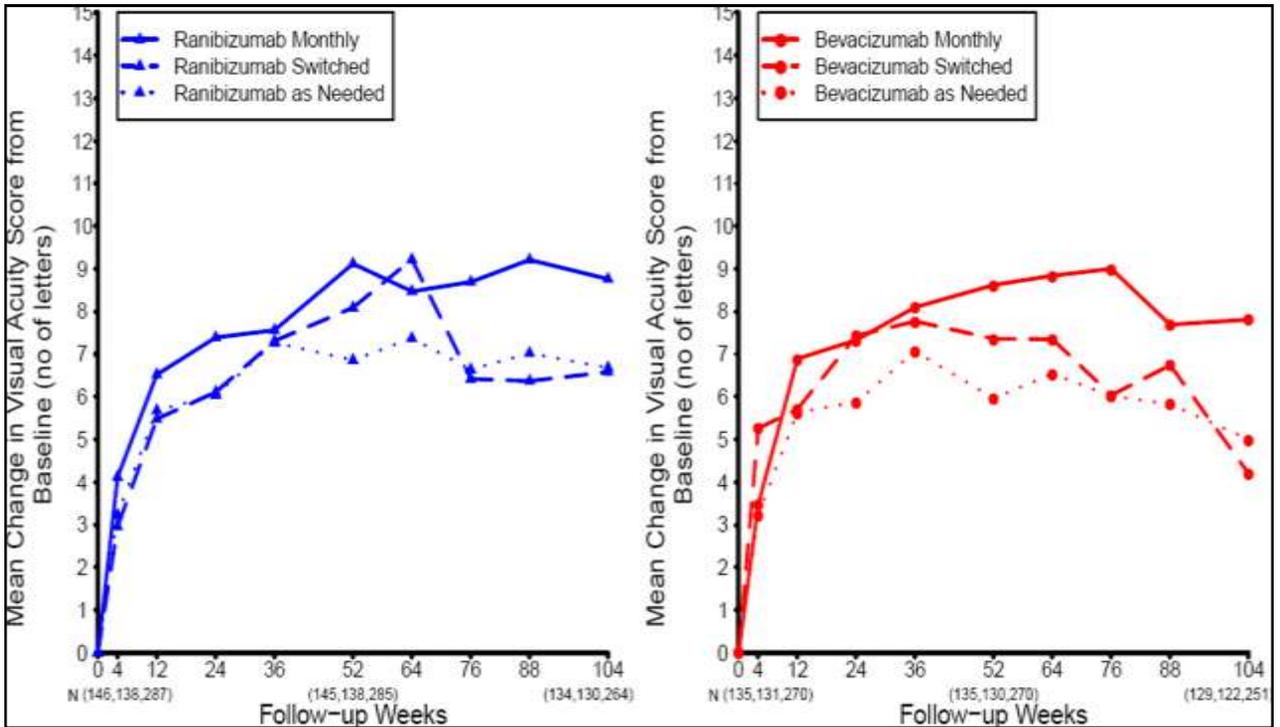
- These vessels are considered a more mature form of the Type 1 lesion, which may explain varying degrees of **anti-VEGF resistance**.
- Although anti-VEGF therapy often reduces sub-RPE fluid in eyes with polypoidal choroidal vasculopathy, **the aneurysmal lesions often persist**.



III. Treating The Fluid



Neovascular Fluid



- Multiple clinical trials such as HARBOR, VIEW1&2 and HAWK and HARRIER Brucizumab trials demonstrated that protocols tolerating subfoveal SRF had similar visual outcomes compared with protocols not tolerating any SRF.
- Tolerating SRF to some extent led to fewer injections at 12 and 24 months.



Non-neovascular Fluid



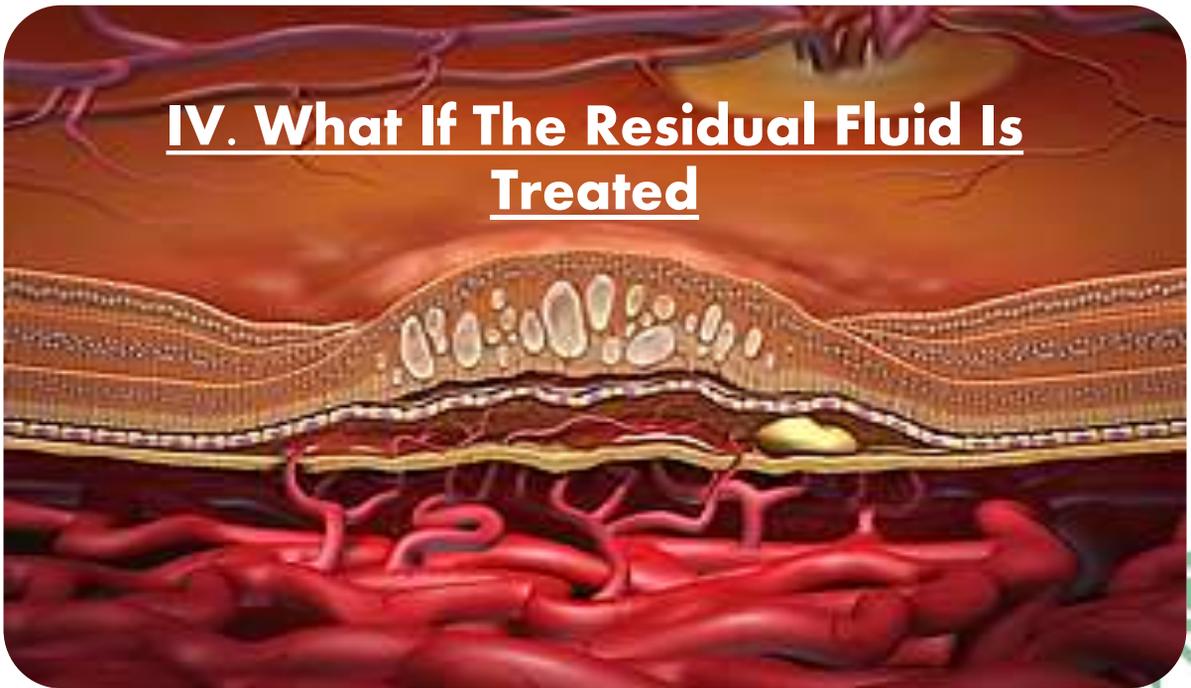
- Santina et al recently proposed an **“observe and extend”** protocol for the management of non-neovascular SRF.
- The natural history of non-neovascular fluid is **long-term stability/spontaneous resolution** in those eyes that developed iRORA/cRORA.
- Vigilance is critical because **any progression** of fluid, decline in vision, or detection of MNV with OCTA or identification of other signs of neovascularization should all warrant urgent intervention with anti-VEGF therapy.



- **Choroidal thickness** and morphology should be evaluated in eyes with AMD in which SRF and/or IRF develop, especially in cases with persistent fluid, as the presence of pachychoroid can be a causative or contributory pathway for fluid accumulation in these eyes.
- Treatment options for pachychoroid-associated SRF include PDT and anti VEGFs. Although an observe-and-extend protocol can be considered if the SRF is **mild and stable** and not visually significant, despite the presence of pachychoroid.



IV. What If The Residual Fluid Is Treated



- IVAN study noted that monthly injections of bevacizumab and ranibizumab had a greater likelihood of **developing GA** than the PRN approach.*

*Chakravarthy U, Harding SP, Rogers CA, et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration. Ophthalmology 2012;119:1399–1411

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- Injecting when not definitively beneficial adds to the risk of these drugs being freely available in systemic circulation and may induce **anti-drug antibody formation**.
- Theoretically, anti-drug antibody may render the drug **less effective** and may have a negative outcome when the neovascular lesions will require treatment.

*Chakravarthy U, Harding SP, Rogers CA, et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration. Ophthalmology 2012;119:1399–1411

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- Treating the residual resistant fluid with intensive therapy of anti-VEGFs to achieve anatomical normalcy without any additional functional advantage has an impact on the **economics of healthcare**.
- Furthermore, the **physical and physiological impact** of vision loss represents a significant burden for patients.



Take Home Message



- Biomarkers of activity (fluid, SHRM, heme, progression, OCTA).
- RAP lesions should be treated when needed (PRN).
- PCV lesions → Treat and extend.
- Keep in mind the non-neovascular fluid origins (OCTA is a must).
- In the absence of MNV with OCTA and other features of neovascularization, an observe-and-extend protocol could be considered.
- Pay attention to the choroid.



Thank You