OCT-A Technology and the Growing Importance of Diagnosing and Managing Eye Disease

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Beth Snodgrass, CRA
Ophthalmic Imager
Casey Eye Institute @ OHSU

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OCT Angiography Lesson Objectives

- Define Angiography
- Compare fluorescein angiography to OCT-A
- Explain the technology behind OCT-A
- Look at normal and abnormal OCT-A images
- Overview of OCT-A retinal findings that may correlate with systemic diseases or conditions

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Define Angiography

- *Angio* : blood vessel
- *Gram* : to write or draw
- Angiogram: a rendering of images of blood vessels
  - *Typically, a contrast dye is used to visualize the vasculature*
    - OCT-A is *atypical*

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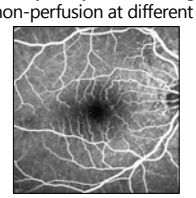
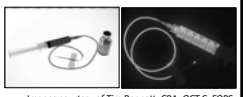
Traditional Fluorescein Angiography
(First FA 1961, Novotny & Alvis)

Purpose: To illustrate retinal circulation

- Retinal fluorescein angiography is a diagnostic timed imaging procedure whereby dye in injected intravenously
  - Results in a 2 dimensional representation of retinal vessels
  - The dye may show leaking, staining, pooling, blocking and / or non-perfusion at different stages of the test





Images courtesy of Tim Bennett, CRA, OCT-C, FOPS

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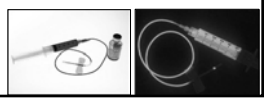
Traditional Fluorescein Angiography
Purpose: To illustrate retinal circulation

- The dye appears and travels through the retinal vessels
  - Documents arm to retina time / 1st appearance of dye
- It is an invasive procedure that has risks
  - Nausea with or without emesis
  - Mild allergic reaction to anaphylaxis (rare)
- Contraindicated in pregnancy and breast-feeding



Images courtesy of Tim Bennett, CRA, OCT-C, FOPS

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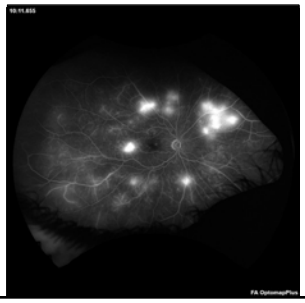
Traditional Fluorescein Angiography

- IVFA and ICG cameras have several fields of view
  - 20 degree to 180 degrees

Optos Wide Field Camera
17 seconds - Arterial Phase; Choroidal Flush
24 seconds – Laminar Flow
30 seconds – A/V Filling; NVE, non-perfusion, micro-aneurysms
5 minutes – Mid Phase; NVE leakage
10 minutes – Late Phase; more profuse NVE leakage with vasculitis



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Traditional Fluorescein Angiography

Challenges with IVFA

- Patient's inability to tolerate bright lights (photophobia)
- Fear of needles / Vaso-vagal response to needles
- Poor venous access
  - May require multiple sticks or waiting for IV Team to place a line
  - Extravasation of dye from the vein into the tissue
- May take up to 20-30 minutes from prepping the dye, consenting the patient, dye injection to completion of the final phase of the angiogram

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OCT Angiography

(first described in 2006, Shuichi Makita *et al*)

Purpose: To illustrate retinal blood flow of normal eyes and those with vascular anomalies, non-perfusion and neovascularization

- Contrast dye is not required
- Non-invasive, non-contact imaging
- Uses infrared light (840 nm to 1050 nm)
- Capture time in a cooperative patient without opacities takes about 10 minutes
- Clinical OCT-As have a 10 to 30 degree field of view[4]
  - Up to 100 degree montage image
  - Extreme retinal peripheral vessels are not accessible
  - Newer OCT-A technology may not require montage for wider field of view

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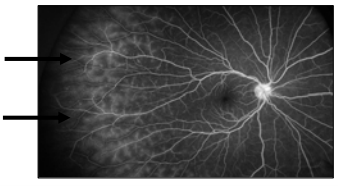
OCT Angiography

- Unable to assess dye appearance time or arterial / venous filling
- OCT-A does not illustrate leakage
  - Unable to appreciate vasculitis, leaking blood vessels from inflammation
- Image artifacts may be problematic in quantifying data and interpreting results, sometimes requiring physician interaction[10]



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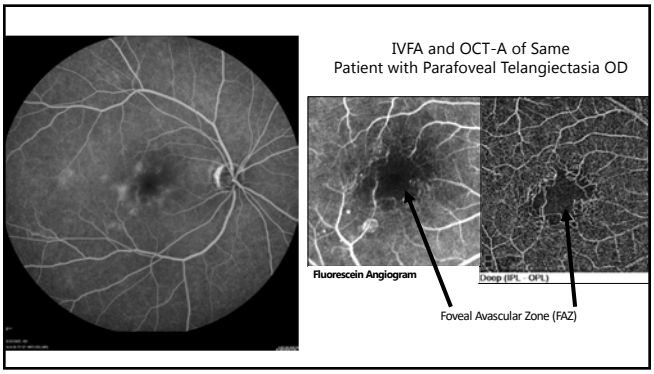
IVFA and OCT-A of Same
Patient with Parafoveal Telangiectasia OD
Fluorescein Angiogram
Deep (IPL - OPL)
Foveal Avascular Zone (FAZ)

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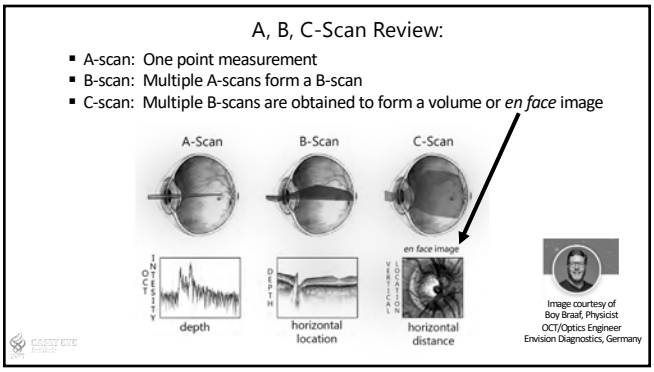
A, B, C-Scan Review:
A-scan: One point measurement
B-scan: Multiple A-scans form a B-scan
C-scan: Multiple B-scans are obtained to form a volume or en face image
A-Scan
B-Scan
C-Scan
en face image
OCT INTENSITY
depth
DEPTH
horizontal location
VERTICAL LOCATION
horizontal distance
Image courtesy of
Boy Braaf, Physicist
OCT/Optics Engineer
Envision Diagnostics, Germany

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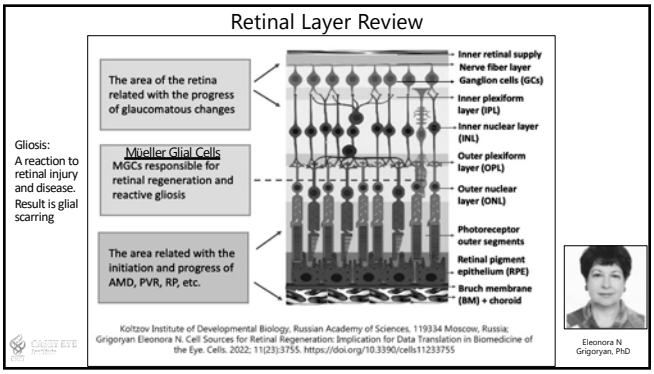
Retinal Layer Review
Gliosis:
A reaction to retinal injury and disease.
Result is glial scarring
The area of the retina related with the progress of glaucomatous changes
Müeller Glial Cells
MGCs responsible for retinal regeneration and reactive gliosis
The area related with the initiation and progress of AMD, PVR, RP, etc.
Inner retinal supply
Nerve fiber layer
Ganglion cells (GCs)
Inner plexiform layer (IPL)
Inner nuclear layer (INL)
Outer plexiform layer (OPL)
Outer nuclear layer (ONL)
Photoreceptor outer segments
Retinal pigment epithelium (RPE)
Bruch membrane (BM) + choroid
Koltzov Institute of Developmental Biology, Russian Academy of Sciences, 119334 Moscow, Russia;
Grigoryan Eleonora N. Cell Sources for Retinal Regeneration: Implication for Data Translation in Biomedicine of the Eye. Cells. 2022; 11(23):3755. https://doi.org/10.3390/cells11233755
Eleonora N Grigoryan, PhD

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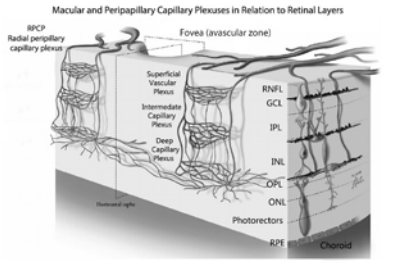
Macular and Peripapillary Capillary Plexuses

Plexus: A network of anastomosing or interlacing blood vessels (or nerves)

Greek - "to braid"



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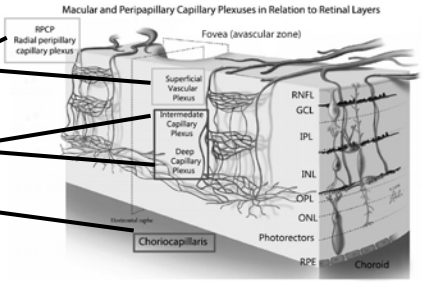
Macular and Peripapillary Capillary Plexus Grouping in OCT-A[1]

Superficial Vascular Complexes

Deep Vascular Complexes

Choriocapillaris



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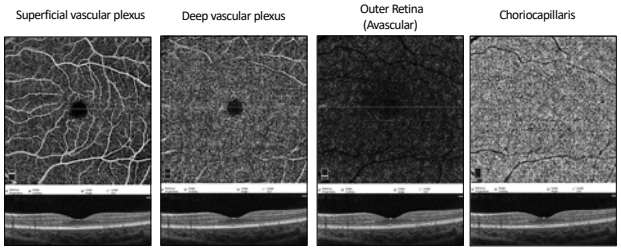
Retinal Vascular Plexus (6 x 6) Corresponding B-scans with Flow Overlays



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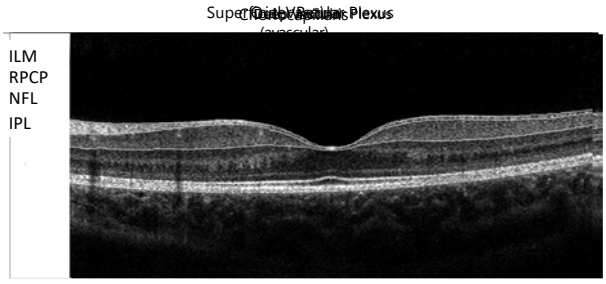
Optovue Retinal Vascular Plexus 6 x 6 with Segmentation Lines



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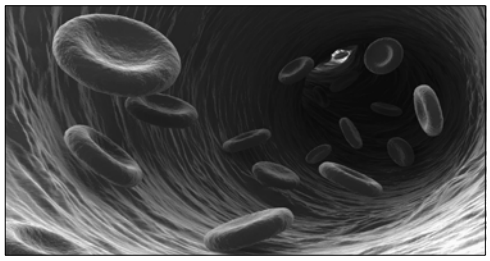
More on Motion Contrast: How do they track those RBCs?



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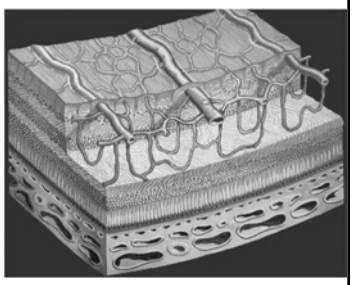
OCT Angiography

- OCT angiography uses motion contrast to render blood vessels
  - Utilizes the signal difference between
  - blood flow
  - stationary tissue



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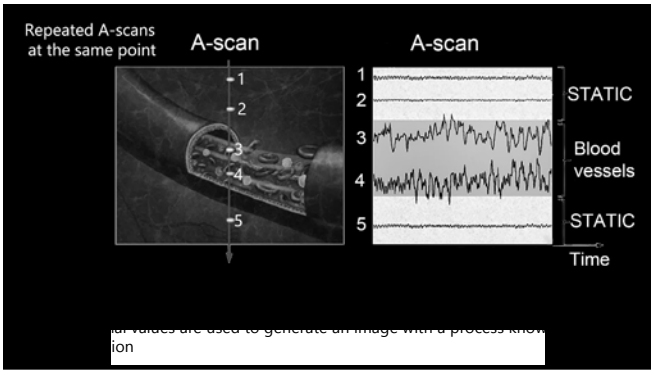

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Signal to Noise Ratio
High signal from RBCs
Low signal from tissue
Decorrelation clears out the noise

$$SNR = \frac{P_{signal}}{P_{noise}}$$

Red Blood Cells
Wanted component

Surrounding Tissue
Unwanted component

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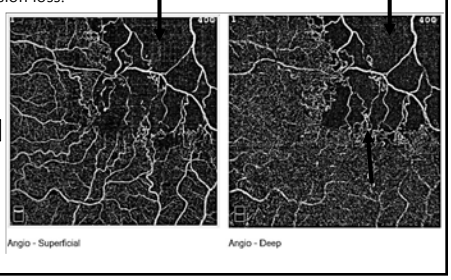
- OCT-A is a metabolic rendering of the retina (OCT is structural)
  - Proper retinal metabolic performance demands oxygen
    - Reduced oxygen may cause apoptosis, cell death, esp. to neural tissue, resulting in vision loss. [2]

BRVO OS
Visual Acuity
OD 20/30
OS 20/70+2

Non-perfusion and collaterals



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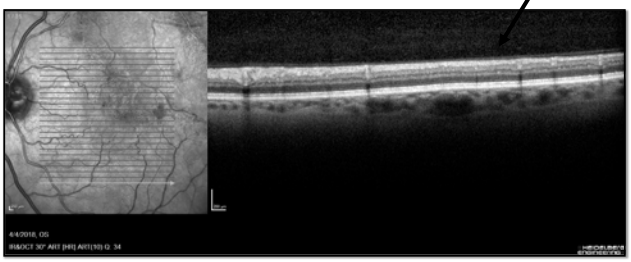
Superior edema is seen on OCT, not on OCT-A



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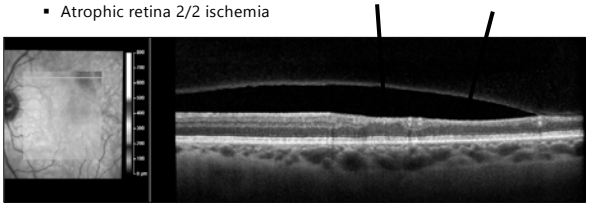
BRVO OS 4 months later after anti-VEGF injections

- Proper retinal performance demands oxygen
  - Reduced oxygen may cause cell death, esp. to neural tissue, resulting in vision loss.[2]
  - Atrophic retina 2/2 ischemia



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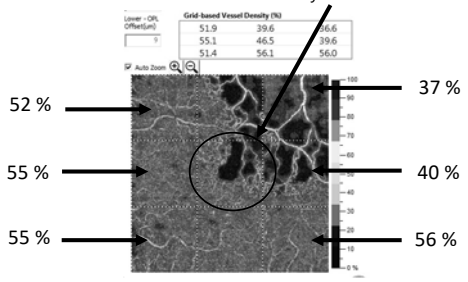
OCT-A Vessel Density quantifies lack of flow

Deep Plexus: Grid Based Vessel Density %
Parafoveal vessel density = 46.5%



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Glaucoma: Thinning Retinal Nerve Fiber & Damaged Ganglion Cells
These cells assist in transmitting retinal stimuli
to the brain via the optic nerve

Several Mechanical Causes:

- High IOP damages RNFL
  - Too much aqueous fluid production
  - Blockage of Schlemm's canal – 'outgoing plumbing'
    - Pigment
    - Exfoliation
    - Neovascularization in the angle
  - Uveitis (vasculitis)
  - Some medications
  - Congenital
  - Trauma

Compromised Vascular Supply:

- RNFL blood supply is the RPCP (Radial Peripapillary Capillary Plexus)
- Ganglion cells are in the macula and are supplied by the SVP (Superficial Vascular Plexus)

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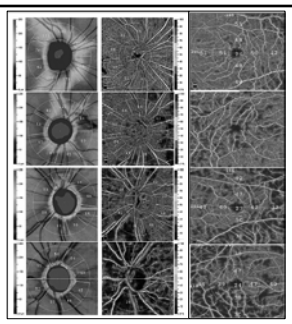
Vessel Densities of Radial Peripapillary (RPCP)

Normal Optic Nerve

Mild POAG

Moderate POAG

Severe POAG



Vessel Densities Superficial Vascular Plexus (SVP)

Capillary loss is noted with OCT-A before visual field changed are documented.

Use at least 6x6 macular scan to evaluate glaucoma.

The RPC and macular vascular vessel density showed a significant correlation with the degree of glaucoma severity.[12] *Al-Nashar Haitham Y, et al.*[19]

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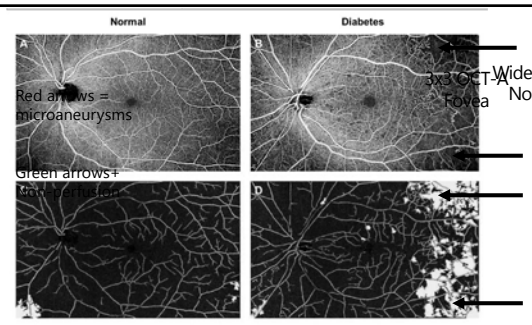

Optical Coherence Tomography Angiography in Diabetes and Diabetic Retinopathy. *Journal of Clinical Medicine*. 2020; 9(6):1723.

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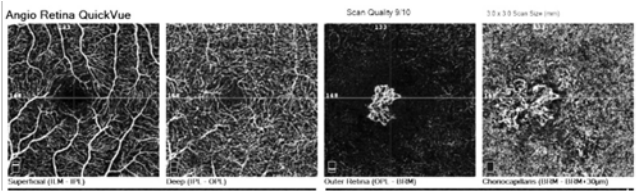
Choroidal Neovascularization (CNV) (type II, 'classic')
2° Macular Degeneration



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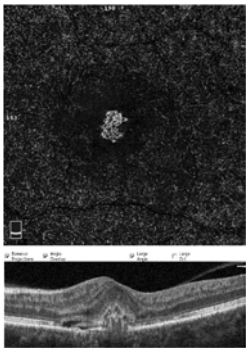
Choroidal Neovascularization
(type II, 'classic")
2° Macular Degeneration



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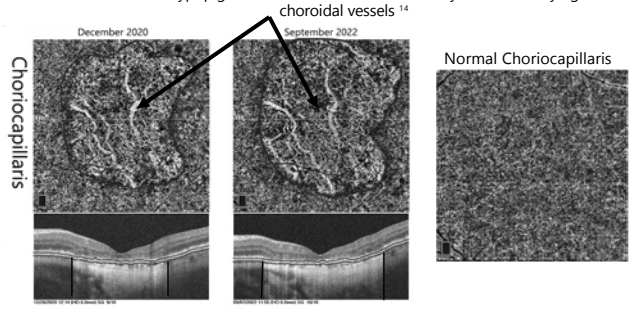
Geographic Atrophy: Late stage dry AMD

Areas of hypopigmentation with increased visibility of the underlying choroidal vessels [14]



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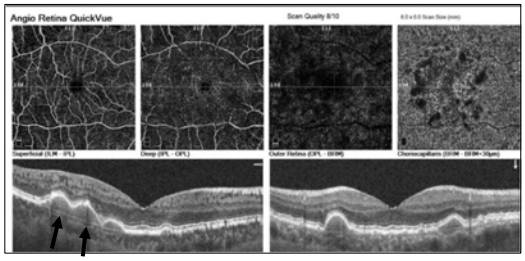
Large Retinal Drusen
2° Macular Degeneration
Looking for vascularized drusen



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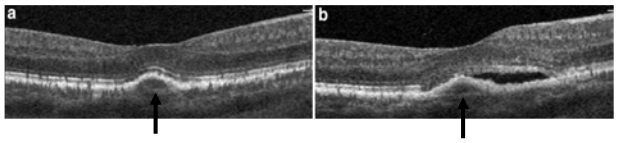
Vascularized Macular Drusen[20]
2° Macular Degeneration



Baseline OCT-A scan showing blood flow at the drusen

Six months later: OCT-A scan showing sub-retinal fluid

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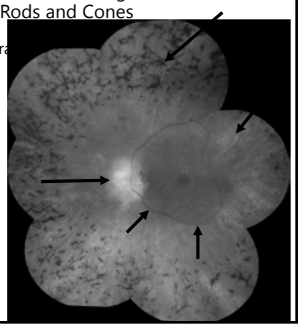
Retinitis Pigmentosa: Inherited Retinal Degeneration of Photoreceptors, Rods and Cones

- Slow, progressive vision loss, starting peripher progressing to central vision loss
  - Night vision loss
  - Field of view constricts over time
  - Bone spicules
  - Attenuated retinal blood vessels
    - Varies with disease progression
  - Atrophic RPE (retinal pigment epithelium)
  - Waxy pallor of the optic disc
  - CME (cystoid macular edema)
  - Several genetic mutations for RP [15]



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Retrospective Clinical Study to Quantify Macular Microvascular Changes in Patients with RP [16]

- 53 patients with RP scanned with OCT-A
  - These images were processed and analyzed with Angio Exercisor software
    - Quantified the microvasculature, vessel density, thickness, length using processes that binarized and skeletonized the original scans
    - Available for research only (Carl Zeiss Meditec)
  - FAZ (foveal avascular zone) was measured using ImageJ software
    - Openly provided by NIH (National Institutes of Health)

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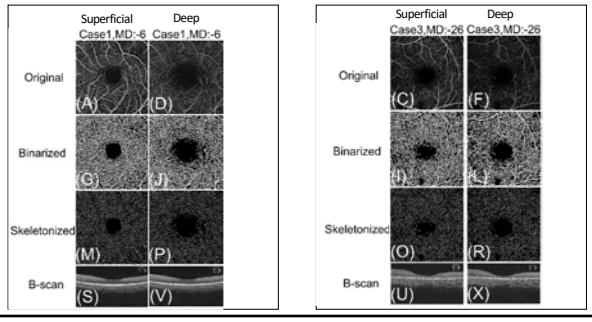
MD = Mean Deviation: Two RP patients Humphrey Visual Field results compared to patients of similar age from the normative database



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Retinitis Pigmentosa With CME

- The pathogenesis of Cystoid Macular Edema in RP is unclear.
- Theories include[17]:
  - Blood-retina barrier breakdown (leakage from compromised blood vessels)
  - RPE (retinal pigment epithelial) pump failure
  - Müeller cell failure
    - Cells that regulate homeostasis within the retinal tissue
    - Oxidative stress and inflammation associated the degenerating retina may result in macular edema

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Retinitis Pigmentosa
With CME

- Another retrospective study of 42 patients with RP scanned with OCT-A[17]
  - The authors suggest that the CME may not be from leaky blood vessels, but from malfunctioning Müeller cells
  - Müeller cells regulate retinal tissue osmosis
  - RP-CME was located in the INL (Inner Nuclear Layer) in the parafoveal macula of the Deep Plexus

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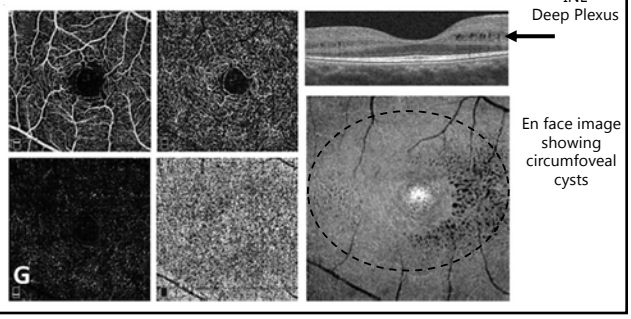
Retinitis Pigmentosa
With Mild CME



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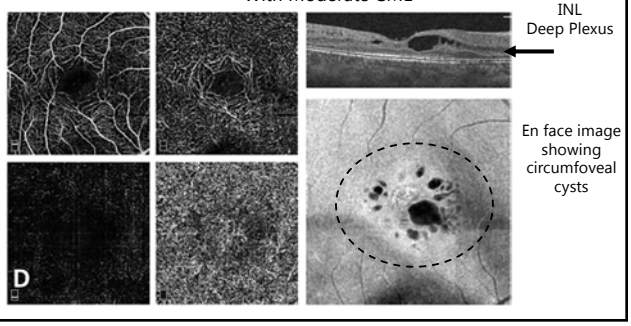
Retinitis Pigmentosa
With Moderate CME



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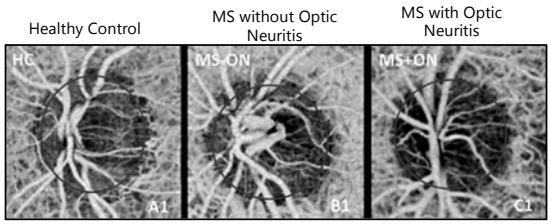
A Few Systemic Correlations Made with OCT-A
Multiple Sclerosis



Optical coherence tomography angiography of optic nerve head and parafovea in multiple sclerosis,Xiaogang Wang et al. Br J Ophthalmol 2014;98:1368-1373

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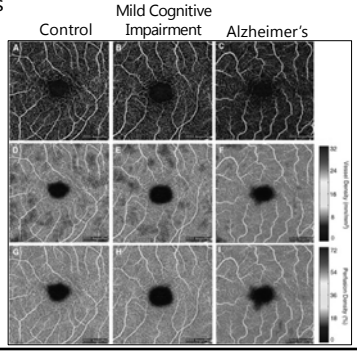
Alzheimer's



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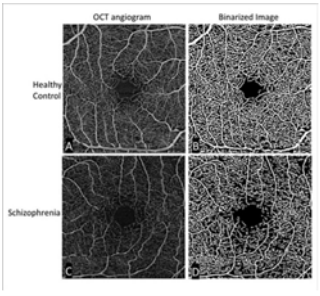
A Few Systemic Correlations Made with OCT-A
Schizophrenia



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OCT-A and Associated Artifacts[10]

- Human :
  - Eye Movements / Saccades / Blinking
    - Motion detection technology uses a two-level approach to:
      1. real-time correction for rapid eye movements or blinking
         a) 'eye-tracker'
      2. Post-processing correction of smaller motion artifacts
  - Poor focus / dry eyes
    - Instilling moisturizing drops for every patient may help the patient hold blinks during the scan
  - Poor fixation
    - So poor that eye trackers cannot resolve

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Signal strength is, in part, dependent on the OCT-A operator

- Focus, focus, focus!
- Patient positioning
  - We want them to hold still
  - Avoid head tilt
- Instill moisturizing drops
  - We want them to hold blinks for several seconds
- Educate & coach your patient through the capture process
- Sometimes, you can only get what you can get

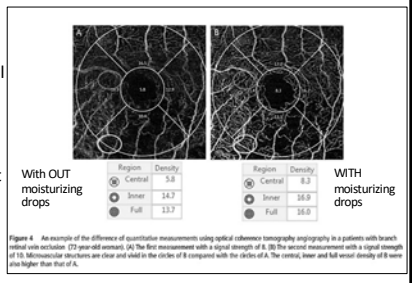

Figure 4 An example of the difference of quantitative measurements using optical coherence tomography angiography in a patients with branch retinal vein occlusion (72-year-old woman). (A) The first measurement with a signal strength of 8. (B) The second measurement with a signal strength of 10. Microvascular structures are clear and vivid in the circles of B compared with the circles of A. The central, inner and full vessel density of B were also higher than that of A.

Lee M, Kim K, Lim H, *et al*. Repeatability of vessel density measurements using optical coherence tomography angiography in retinal diseases, *British Journal of Ophthalmology* 2019;**103:**704-710.

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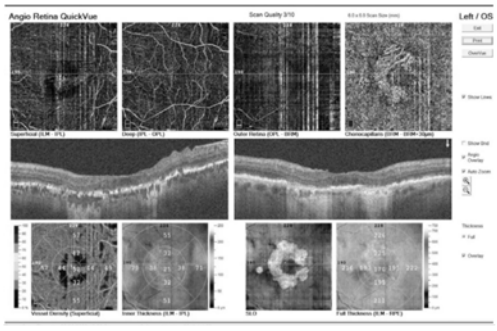
Geographic Atrophy patient with poor fixation



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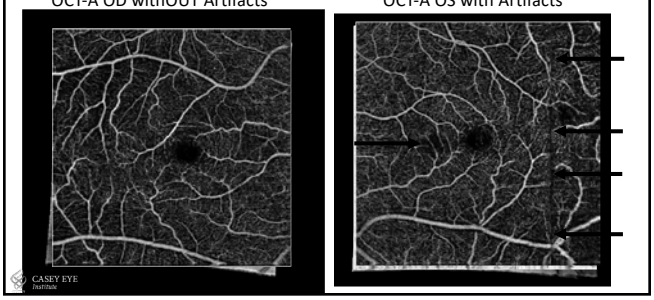
Motion Contrast and Associated Artifacts

OCT-A OD withOUT Artifacts

OCT-A OS with Artifacts



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OCT-A and Associated Artifacts[10]

- Inherent Properties and Pathology of the Eye
- Floaters
  - Shadows the OCT beam blocking its passage to the deeper layers of the retina/choroid
  - May understate blood flow / blood volume (false negative)
    - Prior to scanning, ask the patient move their eyes right to left or up & down to see if the floaters will move away from the macula / nerve
  - Cataracts
    - Full dilation may help the image navigate around opacities

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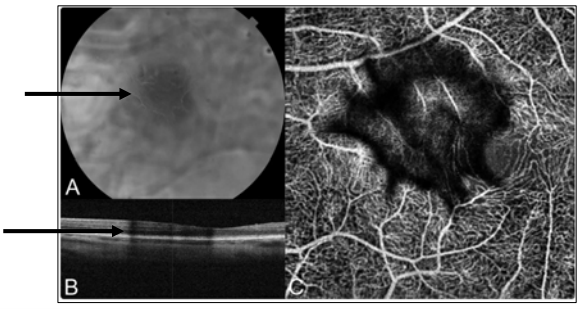
Large Vitreous Opacity or Floater

Blocks the OCT-A signal



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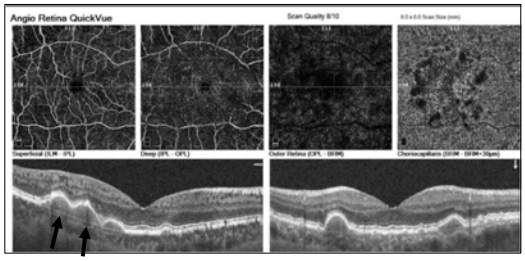
Large Retinal Drusen
2° Macular Degeneration
The drusen block the signal, creating a false negative for choriocapillary blood flow



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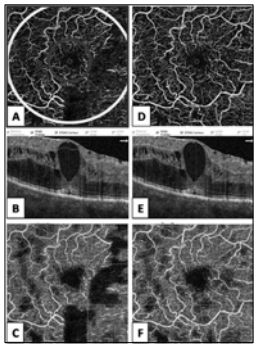
Segmentation Errors



Falavarjani , et al
http://orcid.org/0000-0001-5721-1844

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OCT-A and Associated Artifacts[10]

- OCT-A Projection Artifacts
  - Light reflected from moving blood cells is the basis of OCTA.
  - The light that has passed through moving blood also encounters tissue below the blood vessel
- When this light strikes the RPE it is reflected back to the OCT instrument, misrepresenting blood vessel that particular retinal layer
  - Projection artifacts occur from superficial retinal vessels to the deeper retinal layers
    - These artifacts are nearly always present and appear in any structure that is located below vasculature

Image Artifacts in Optical Coherence Angiography
Spaide, et al

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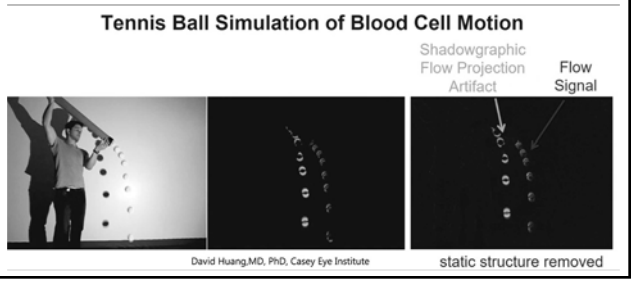
OCT-A and Associated Artifacts[19]

Tennis balls are RBCs. Algorithm removes stationary structures.
Flow signal and shadow / projection artifacts remain



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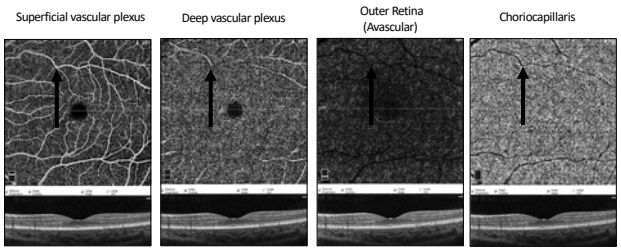
Retinal Vascular Plexus
(6 x 6) Corresponding B-scans with Flow Overlays



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In Summary

- OCT-A is a relatively new diagnostic tool that enhances our ability to observe ocular vasculatures, including blood flow, vessel volume, and vessel anomalies.
- It's technology is intriguing in that it does not require contrast dye, but renders vessel images with red blood cells
- It has clinical and research applications to improve our understanding of disease processes and to consider introducing new biomarkers for disease.
  - Early intervention is BEST!
- Imaging artifacts may require more 'in depth' diagnostic interpretation
  - The degree of image artifact should be reduced

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Thank you!

Beth Snodgrass
snodgrab@ohsu.edu

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References

1. Campbell JP, Zhang M, Hwang TS, Bailey ST, Wilson DJ, Jia Y, Huang D. Detailed Vascular Anatomy of the Human Retina by Projection-Resolved Optical Coherence Tomography Angiography. Sci Rep. 2017 Feb 10;7:42201. doi: 10.1038/srep42201. PMID: 28186181; PMCID: PMC5301488.
2. Richard F. Spaide, James G. Fujimoto, Nadia K. Waheed, Srinivas R. Sadda, Giovanni Staurenghi, Optical coherence tomography angiography, Progress in Retinal and Eye Research,Volume 64,2018,Pages 1-55, ISSN 1350-9462, https://doi.org/10.1016/j.preteyeres.2017.11.003.
3. Country, Michael W. "Retinal Metabolism: A comparative look at energetics in the retina." Brain Research vol. 1672 (2017) 50-57. doi: 10.1016/j.brainres.2017.07.025
4. 3. Borrelli E, Parravano M, Sacconi R, Costanzo E, Querques L, Vella G, Bandello F, Querques G. Guidelines on Optical Coherence Tomography Angiography Imaging: 2020 Focused Update. Ophthalmol Ther. 2020 Dec;9(4):697-707. doi: 10.1007/s40123-020-00286-2. Epub 2020 Aug 1. PMID: 32740741; PMCID: PMC7708612.
5. Chen CL, Wang RK. Optical coherence tomography based angiography [Invited]. Biomed Opt Express. 2017 Jan 24;8(2):1056-1082. doi: 10.1364/BOE.8.001056. PMID: 28271003; PMCID: PMC5330554.
6. Sampson, D.M., Dubis, A.M., Chen, F.K. et al. Towards standardizing retinal optical coherence tomography angiography: a review. Light Sci Appl 11, 63 (2022). https://doi.org/10.1038/s41377-022-00740-9 Published18 March 2022
7. Hormel, T. T., Jia, Y., Jian, Y., Hwang, T. S., Bailey, S. T., Pennesi, M. E., ... & Huang, D. (2021). Plexus-specific retinal vascular anatomy and pathologies as seen by projection-resolved optical coherence tomographic angiography. *Progress in Retinal and eye Research*, *80*, 100878.
8. Gameiro, G.R., Jiang, H., Liu, Y. *et al.* Retinal tissue hypoperfusion in patients with clinical Alzheimer's disease. *Eye and Vis* **5**, 21 (2018). https://doi.org/10.1186/s40662-018-0115-0 Published17 August 2018DOIhttps://doi.org/10.1186/s40662-018-0115-0

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References

9. Lavia C, Bonnin S, Maule M, Erginay A, Tadayoni R, Gaudric A. VESSEL DENSITY OF SUPERFICIAL, INTERMEDIATE, AND DEEP CAPILLARY PLEXUSES USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY. Retina. 2019 Feb;39(2):247-258. doi: 10.1097/IAE.0000000000002413. PMID: 30550527; PMCID: PMC6358199.
10. Spaide RF, Fujimoto JG, Waheed NK. IMAGE ARTIFACTS IN OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY. Retina. 2015 Nov;35(11):2163-80. doi: 10.1097/IAE.0000000000000765. PMID: 26428607; PMCID: PMC4712934.
11. Lee M, Kim K, Lim H, *et al* Repeatability of vessel density measurements using optical coherence tomography angiography in retinal diseases *British Journal of Ophthalmology* 2019;**103:**704-710.
12. Assessment of radial peripapillary capillary and macular vascular density in primary open angle glaucoma Al-Nashar Haitham Y, El-Haig Wael M, Al-Naimy Mohammed A, 2020 | Volume: 113 | Issue Number 2 | Pg.: 46-53
13. Chua J, Sim R, Tan B, Wong D, Yao X, Liu X, Ting DSW, Schmidl D, Ang M, Garhöfer G, Schmetterer L. Optical Coherence Tomography Angiography in Diabetes and Diabetic Retinopathy. *Journal of Clinical Medicine*. 2020; 9(6):1723. https://doi.org/10.3390/jcm9061723
14. Nassisi M, Baghdasaryan E, Borrelli E, Ip M, Sadda SR (2019) Choriocapillaris flow impairment surrounding geographic atrophy correlates with disease progression. PLoS ONE 14(2): e0212563. https://doi.org/10.1371/journal.pone.0212563
15. Retinitis pigmentosa: Clinical presentation and diagnosis; Seema Garg, MD, PhD, Associate Professor, University of North Carolina, Chapel-Hill, Matthew F Gardiner, MD, Associate Professor of Ophthalmology, Harvard Medical School
16. Jauregui, R., Park, K.S., Duong, J.K. *et al.* Quantitative progression of retinitis pigmentosa by optical coherence tomography angiography. *Sci Rep* **8**, 13130 (2018). https://doi.org/10.1038/s41598-018-31488-1
17. Yeo JH, Kim YJ, Yoon YH. OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN PATIENTS WITH RETINITIS PIGMENTOSA-ASSOCIATED CYSTOID MACULAR EDEMA. Retina. 2020 Dec;40(12):2385-2395. doi: 10.1097/IAE.0000000000002756. PMID: 31923123
18. Engelke H, Shajari M, Riedel J, et al OCT angiography in optic disc drusen: comparison with structural and functional parameters,British Journal of Ophthalmology 2020;104:1109-1113.
19. Huang, David, MD, PhD. https://www.aao.org/education/annual-meeting-video/new-diagnostics-what-is-role-of-oct-angiography-i
20. Or, C., Heier, J.S., Boyer, D. *et al.* Vascularized drusen: a cross-sectional study. *Int J Retin Vitr* **5**, 36 (2019). https://doi.org/10.1186/s40942-019-0187-6

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