

Clinical OCT Imaging of Immune Cells in Living Human Eyes with Diabetic Retinopathy

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Celebrating
200
YEARS
1820 - 2020



Ophthalmology Times
Research Scholar
Honoree Program

Disclosures

Maria V. Castanos: None



MY ROLE IN THIS RESEARCH:

- Acquisition of data
- Analysis and interpretation of data
- Creation and/or critical review of the presentation



Richard Rosen



Justin Migacz



Maria Castanos



Davis Zhou

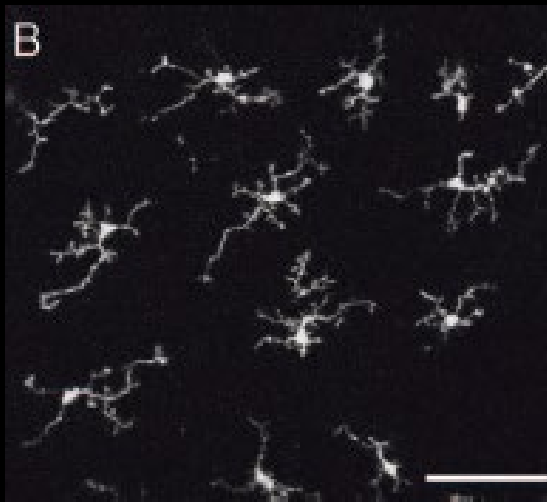


Toco Y.P. Chui

Retinal Macrophages

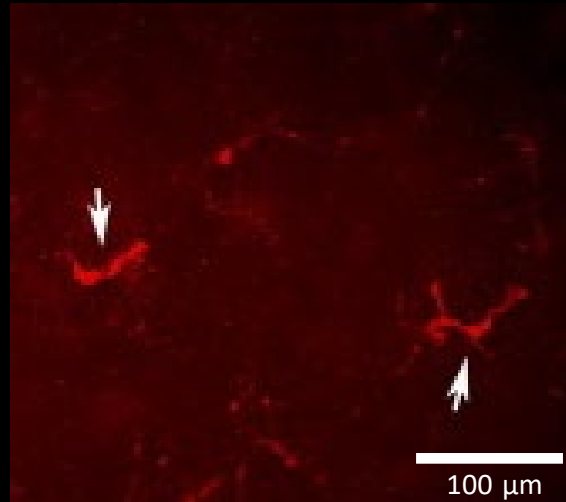
Images below obtained from animal models

Microglia



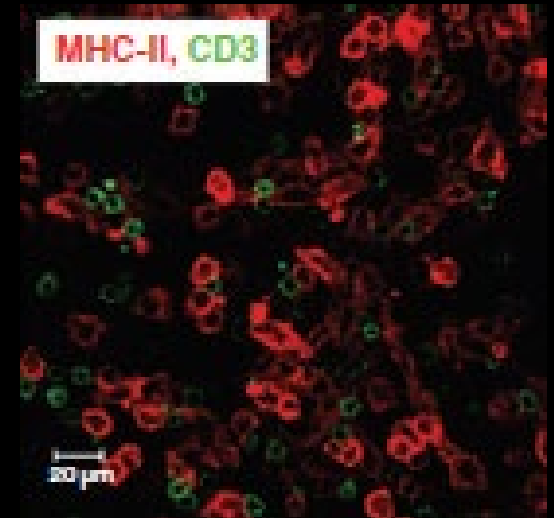
Lee et al. 2008

Hyalocytes



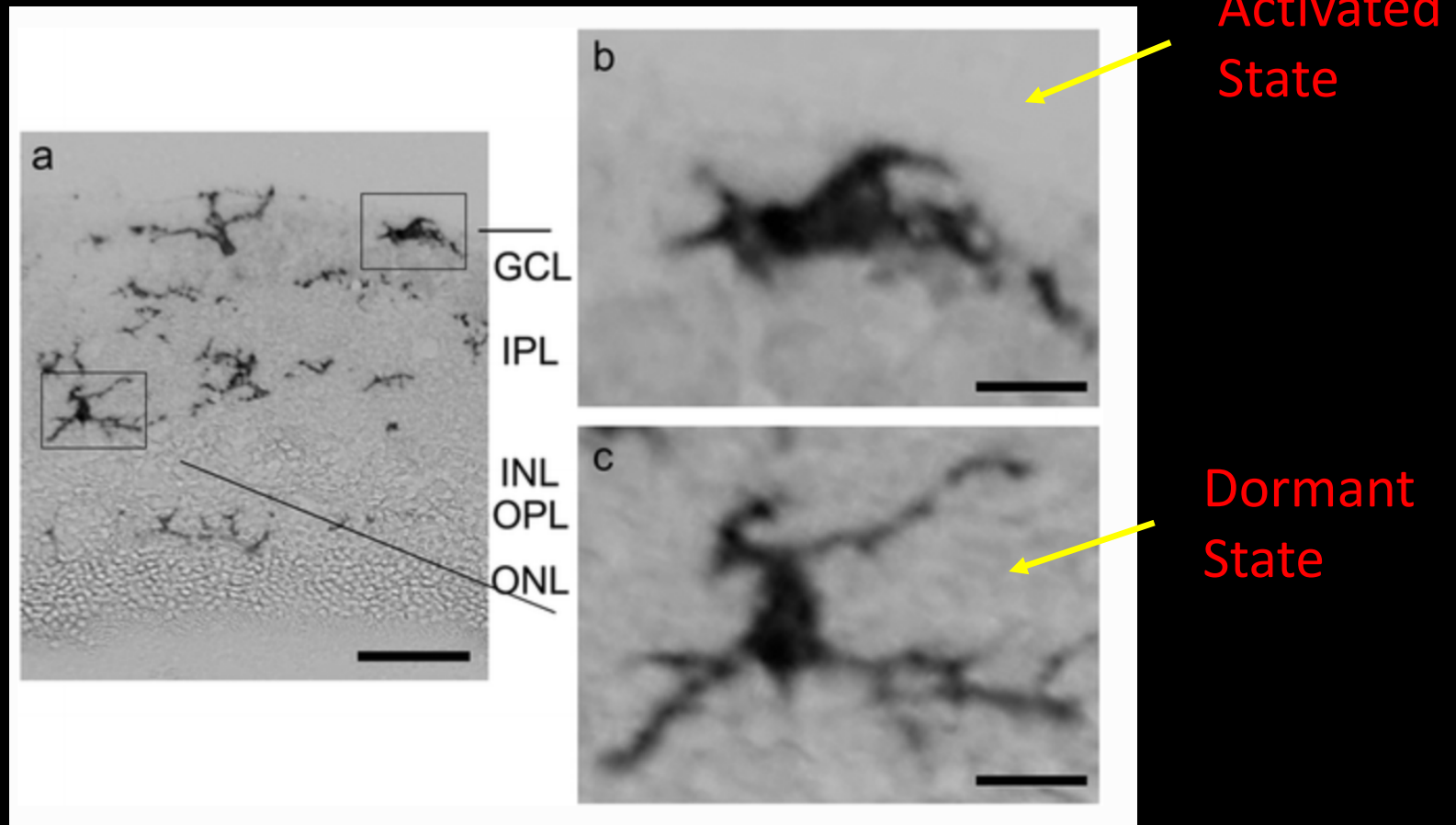
Vagaja et al. 2012

Blood derived Antigen presenting cells



Forrester et al. 2010

Immune cell activation in Diabetes

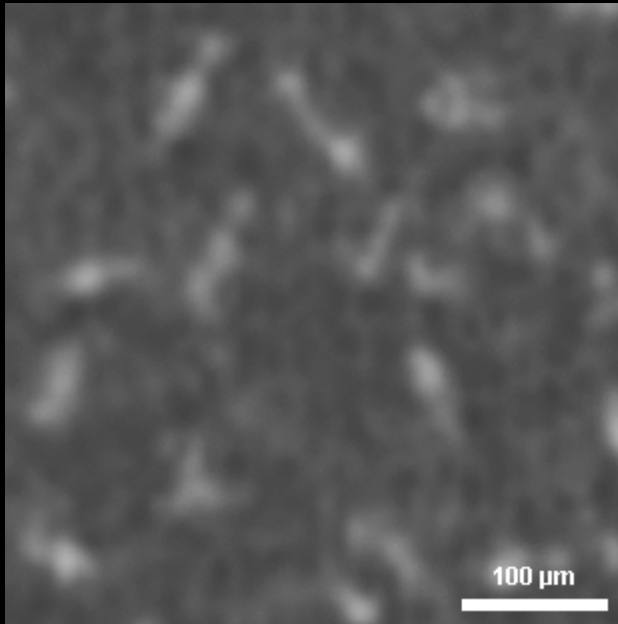


Chen et al, Early spatiotemporal characterization of microglial activation in the retinas of rats with streptozotocin-induced diabetes, Retinal Disorders 2014

Clinical OCT Imaging of Macrophage-like cells

Healthy Controls, Vitreoretinal Interface, Temporal Retina

Clinical OCT

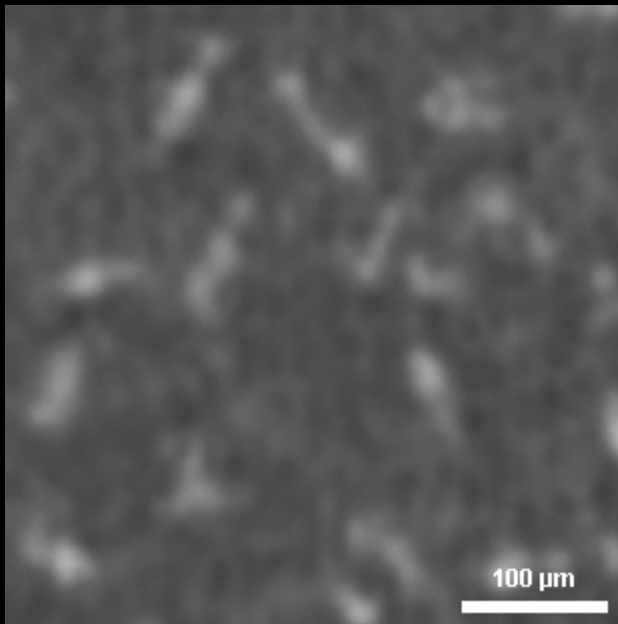


MV Castanos et al., Imaging of Macrophage-Like Cells in Living Human Retina using Clinical OCT, IOVS 2020.

Clinical OCT Imaging of Macrophage-like cells

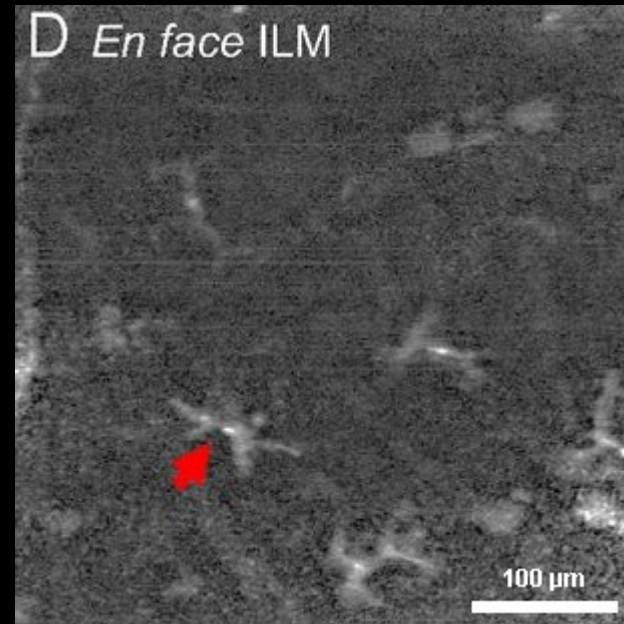
Healthy Controls, Vitreoretinal Interface, Temporal Retina

Clinical OCT



MV Castanos et al., Imaging of Macrophage-Like Cells in Living Human Retina using Clinical OCT, IOVS 2020.

Adaptive Optics - OCT



Z Liu et al., Imaging and quantifying ganglion cells and other transparent neurons in the living human retina, PNAS 2017

DMnoDR



NPDR



PDR



Can clinical OCT be used to visualize macrophage-like cells in diabetic eyes?

Purpose

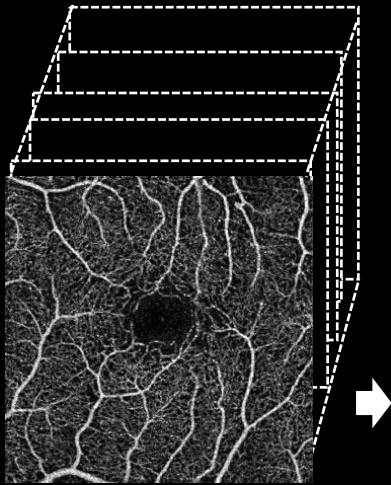
- Image macrophage like cells at the macula of diabetic eyes.
- Compare morphology and distribution of macrophage like cells in healthy vs diabetic eyes
- Evaluate immune cell activity as a biomarker of macular disease and treatment response.

Methods – Image Acquisition and Processing

10 controls, 10 diabetics with different stages of diabetic retinopathy were imaged using a clinical SD-OCT system (Avanti RTVue-XR; Optovue).

1. Optovue Avanti ~10-20 mins

10 Sequential Scans



Enface 3x3mm Macular Scan
OCT-A Full Layer

Healthy Control, 26yo, F

Methods – Image Acquisition and Processing

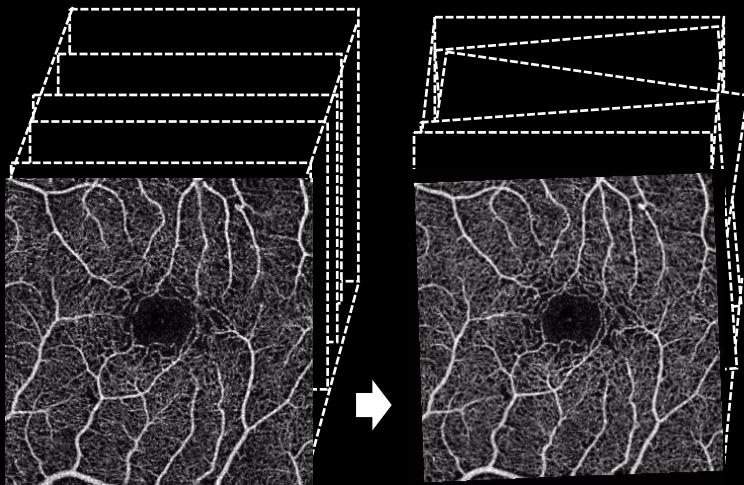
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1. Optovue Avanti ~10-20 mins

2. ImageJ ~5 mins

10 Sequential Scans

Image Registration & Averaging



Enface 3x3mm Macular Scan
OCT-A Full Layer

Register Virtual Stack Slices
Transformation matrix

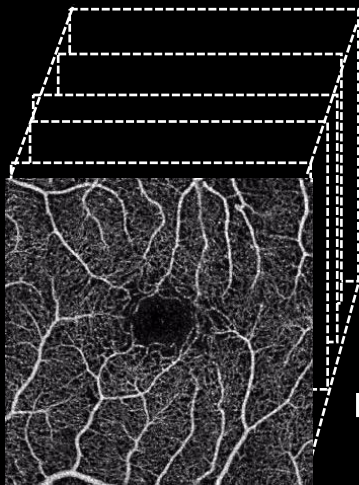
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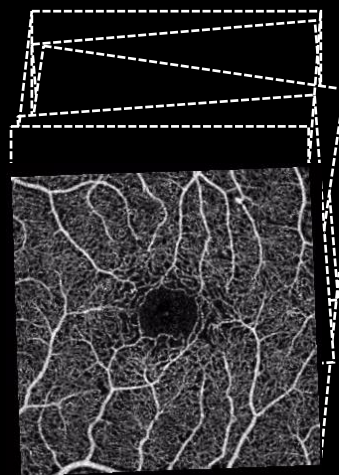
10 Sequential Scans



Enface 3x3mm Macular Scan
OCT-A Full Layer

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Image Registration & Averaging



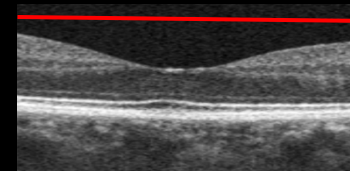
Register Virtual Stack Slices
Transformation matrix

3. Matlab, Optovue, & ImageJ ~3 hrs

3 μm slab OCT-A and OCT-R Stack Registration & Averaging

Apply
Transformation
Matrix

Enface OCT
Angiograph
3 μm slabs



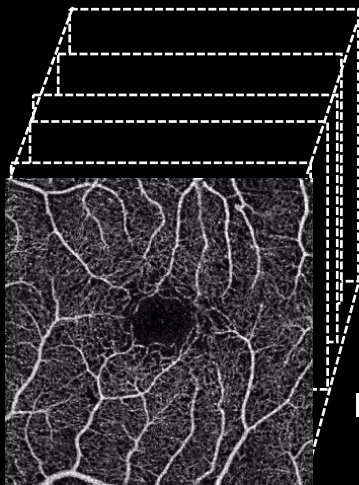
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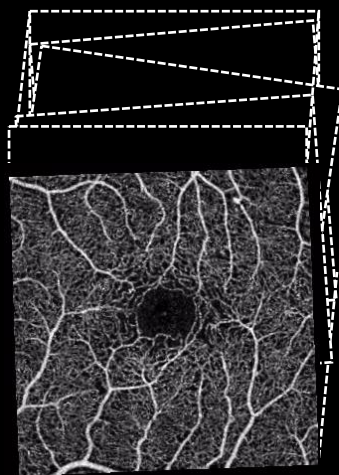
10 Sequential Scans



3x3mm Macular Scan
OCT-A Full Layer

2. ImageJ ~5 mins

Image Registration & Averaging



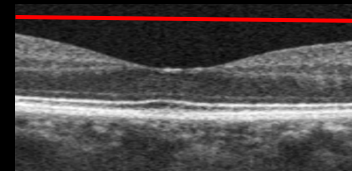
Register Virtual Stack Slices
Transformation matrix

Apply
Transformation
Matrix

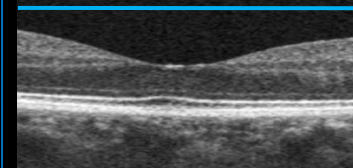
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3 μm slab OCT-A and OCT-R Stack Registration & Averaging

Enface OCT
Angiograph
3 μm slabs



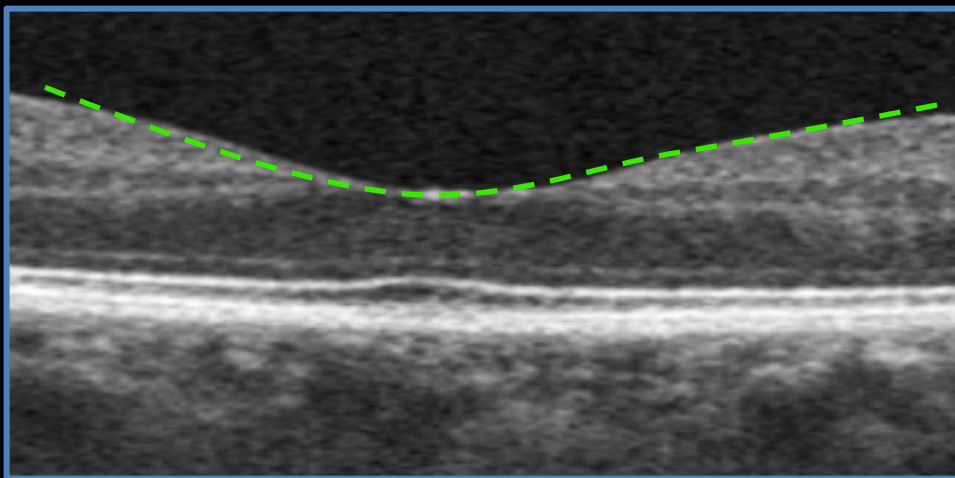
Enface OCT
Reflectance
3 μm slabs



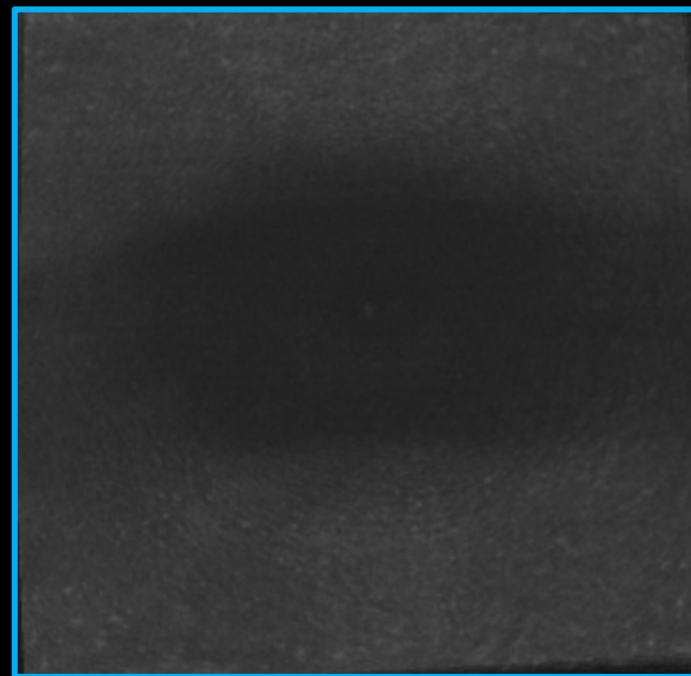
Healthy Control, 26yo, F

Segmentation

Macular 3 μ m Slab
-3 μ m to 0 μ m above the ILM



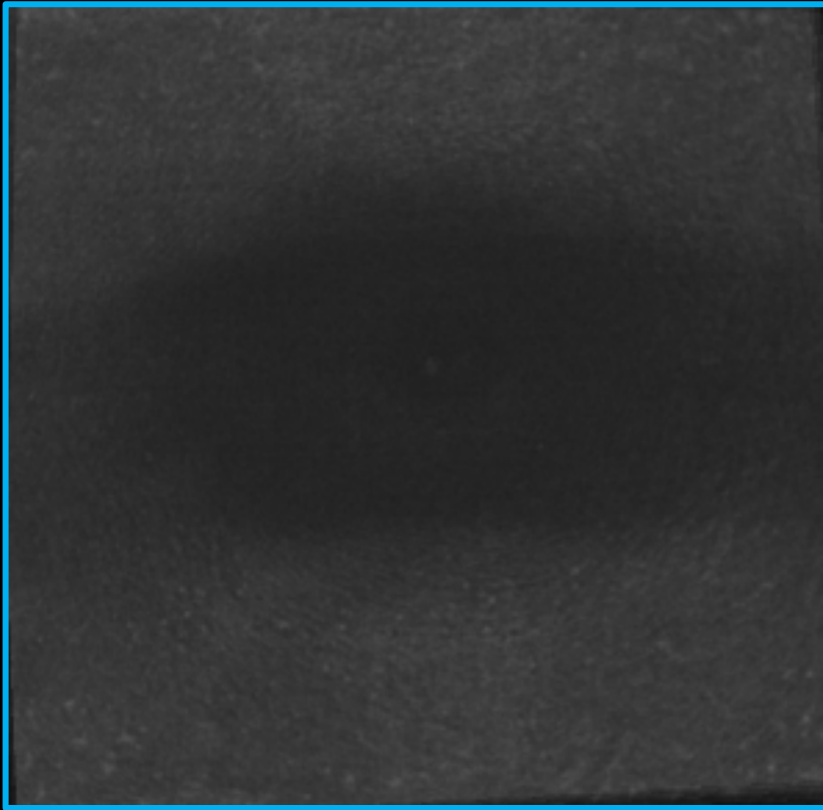
Averaged enface 10 Scans



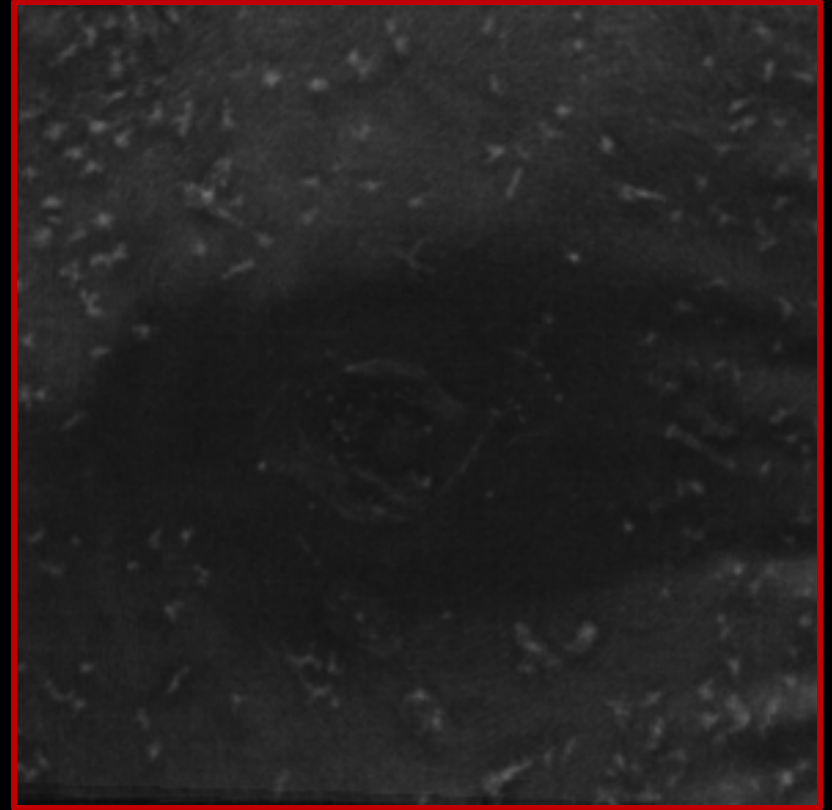
Averaged *enface* OCT- R

3 μ m above the ILM

Control



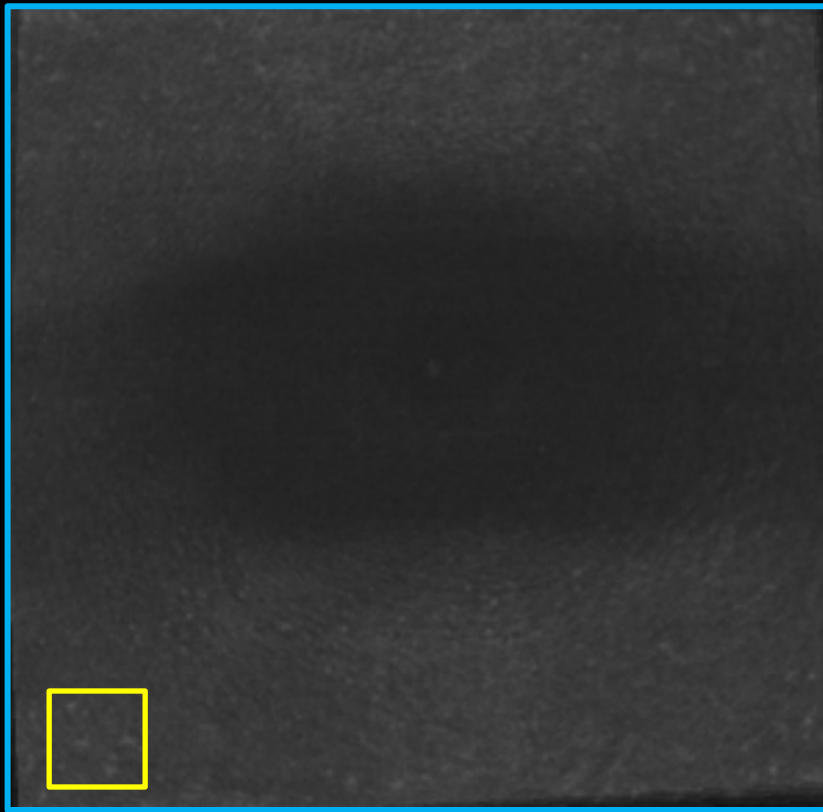
Diabetic



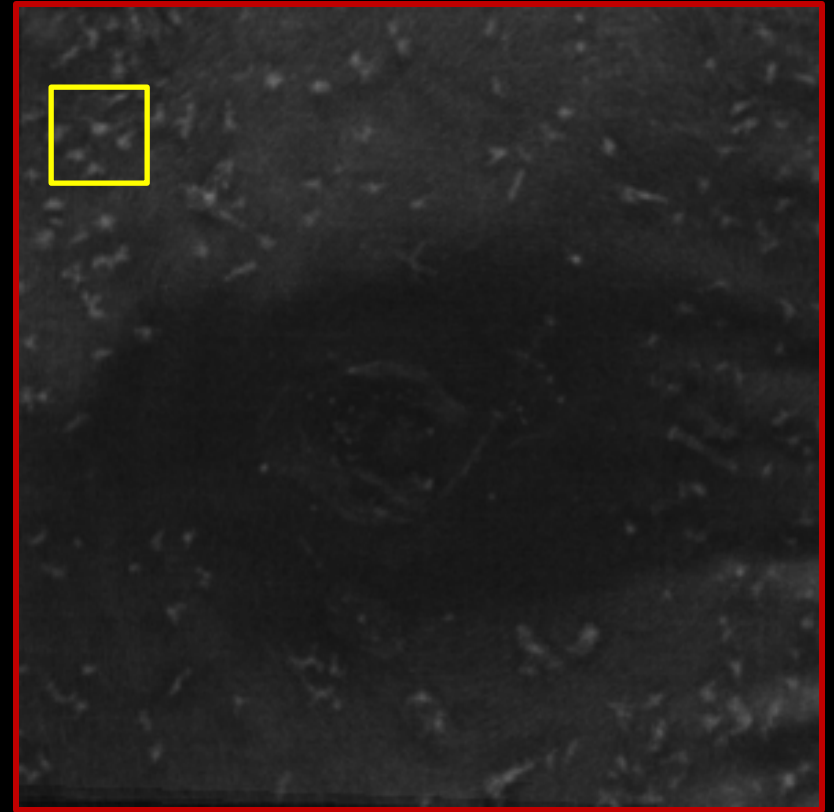
Averaged *enface* OCT- R

3 μm above the ILM

Control



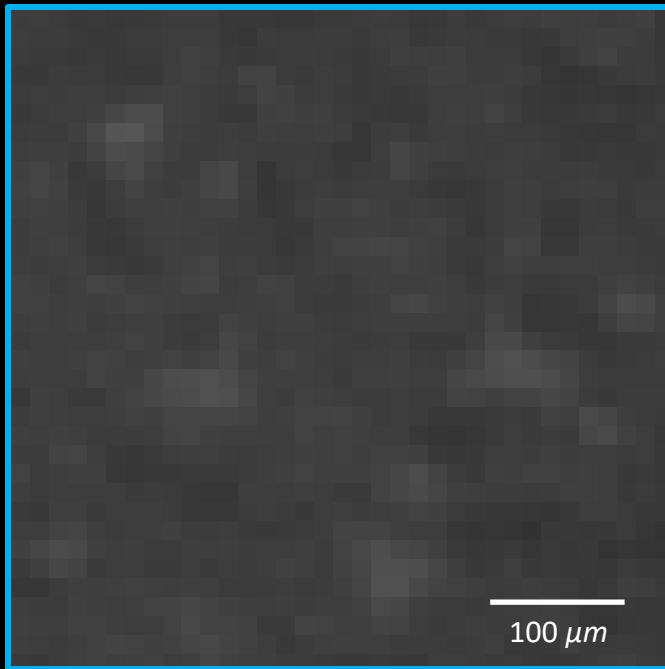
PDR



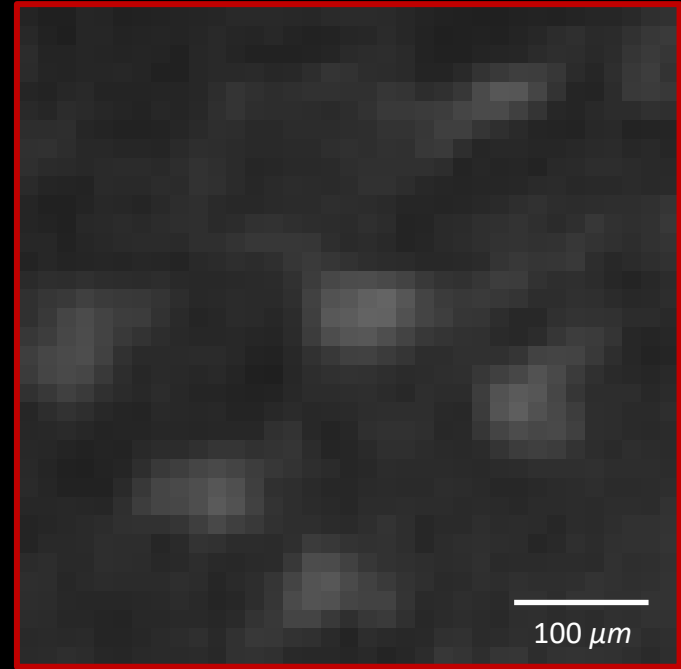
Averaged enface OCT- R

3 μm above the ILM

Control

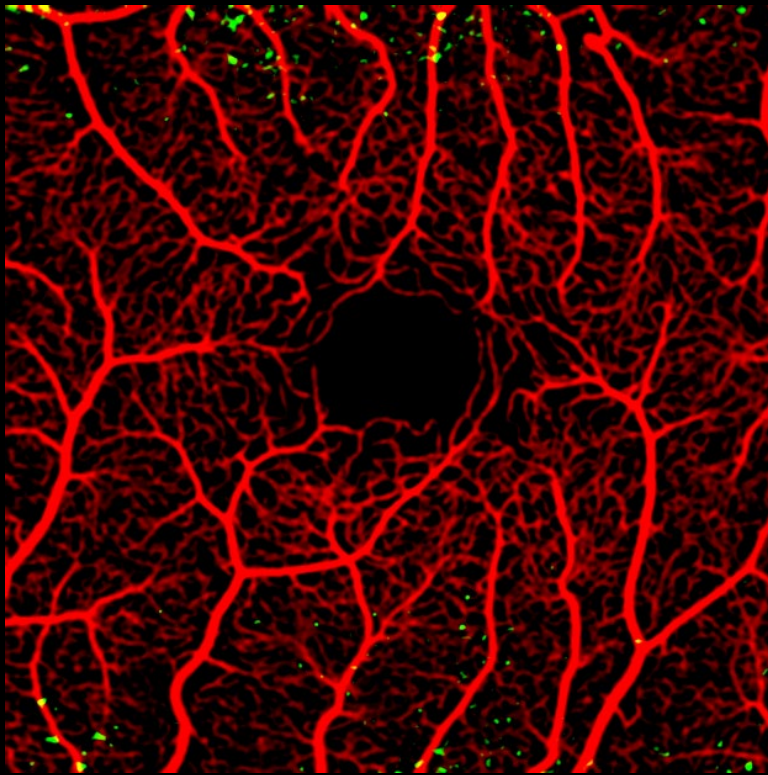


PDR

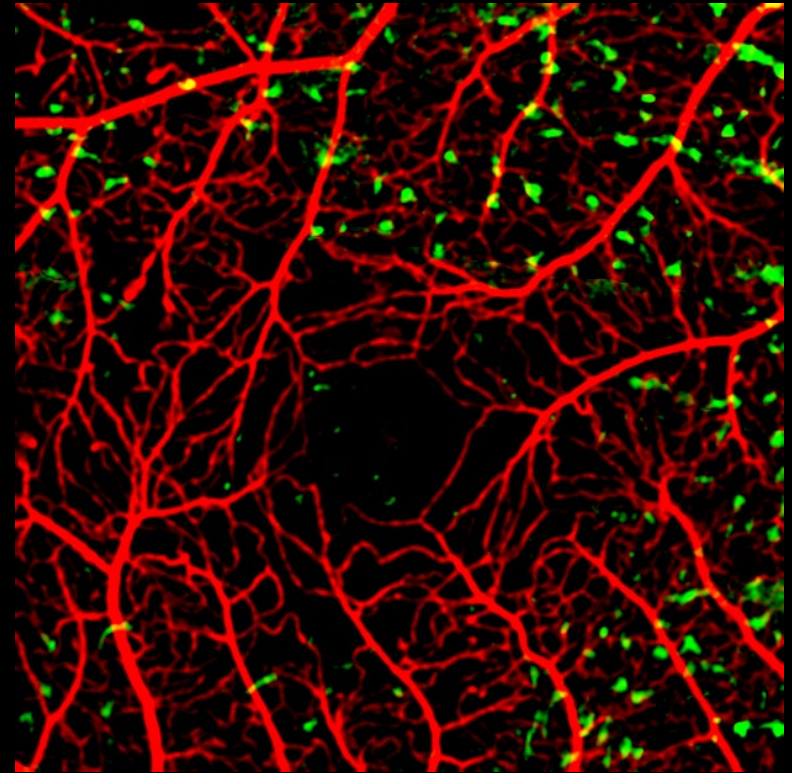


OCT-A and OCT-R overlay

Control



Diabetic

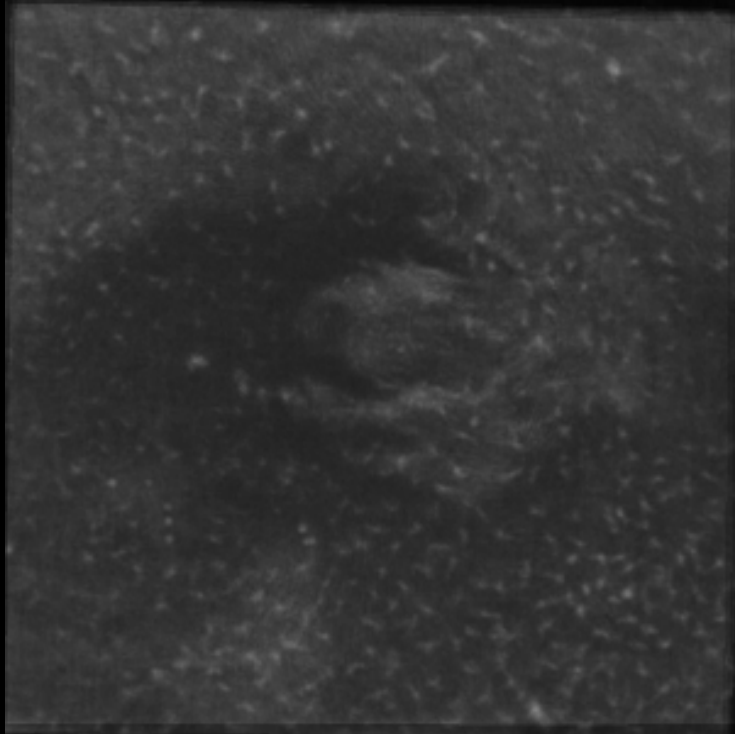


Diabetic Retinopathy- Pre and post Anti VEGF treatment

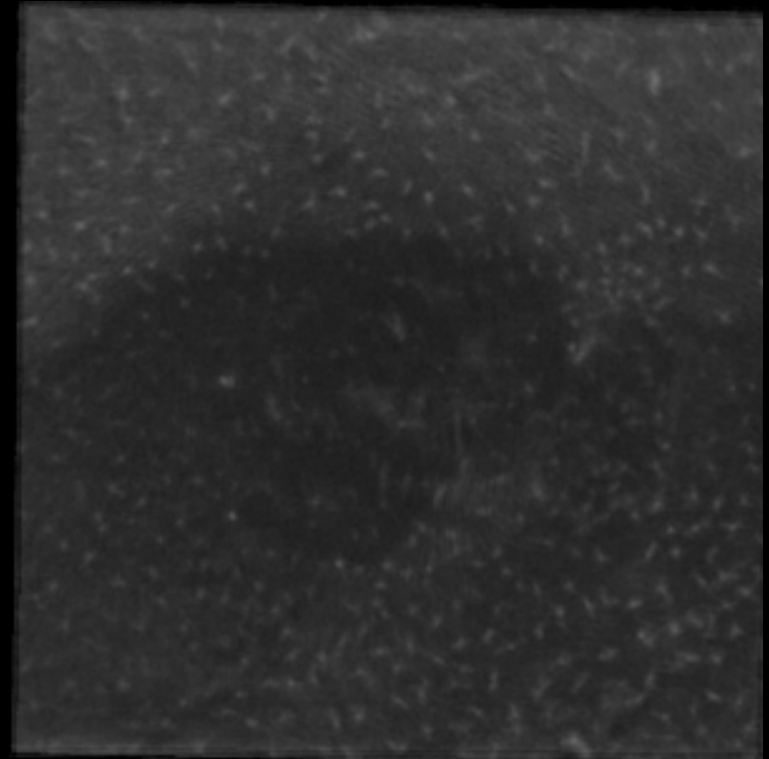
Macula OCT-R, 3 μ m above the ILM

Case 1

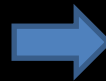
Pre Treatment



Post Treatment



2 weeks after

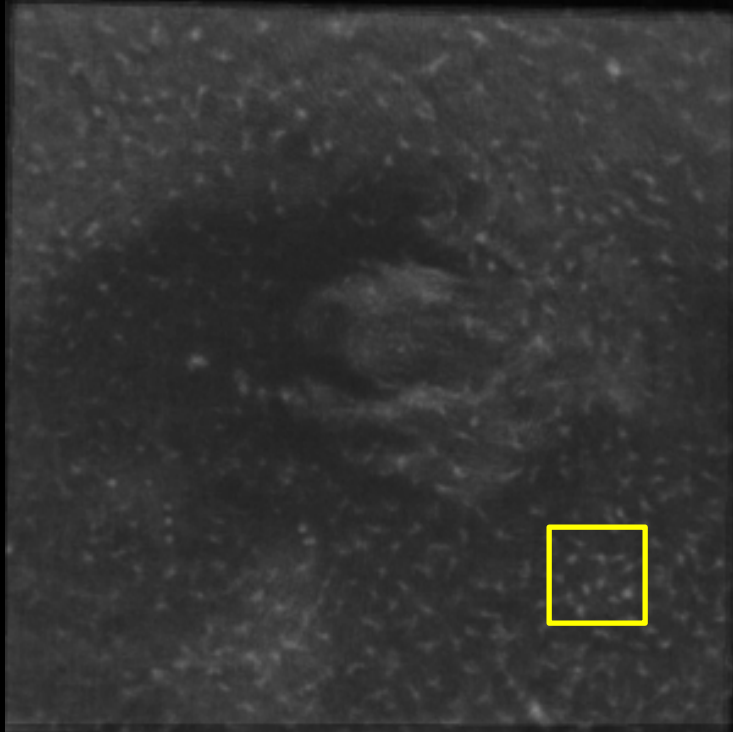


Diabetic Retinopathy- Pre and post Anti VEGF treatment

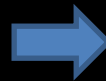
Macula OCT-R, 3 μ m above the ILM

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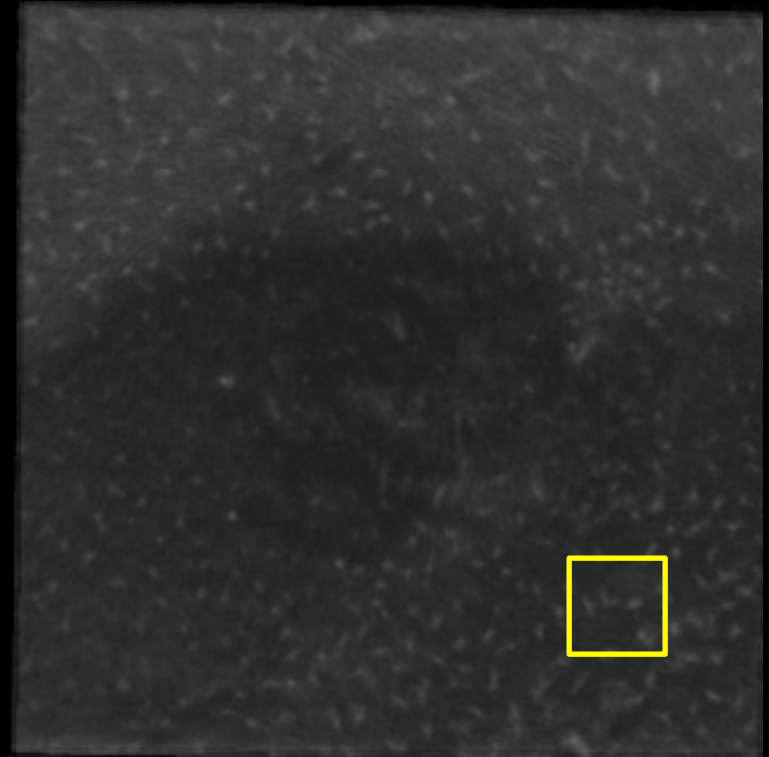
Pre Treatment



2 weeks after



Post Treatment

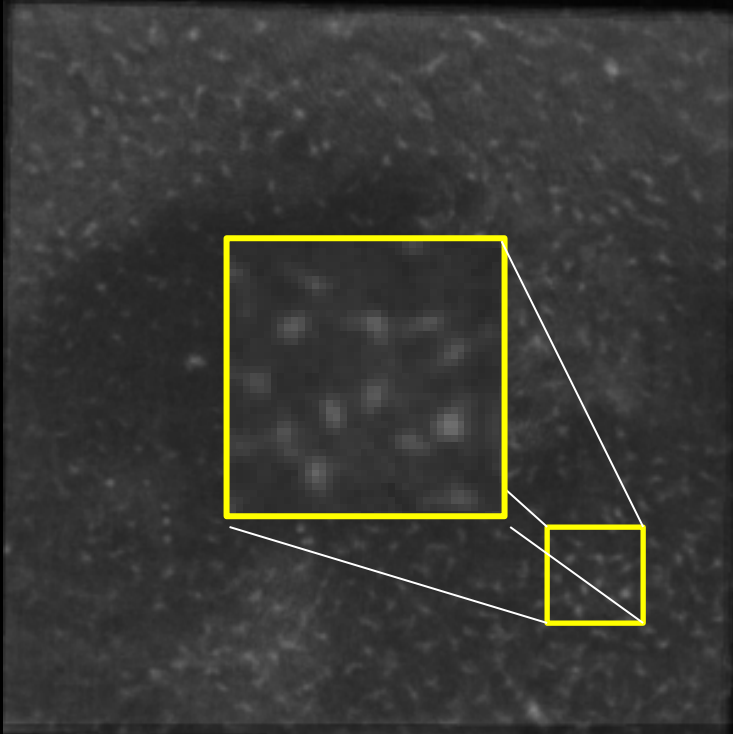


Diabetic Retinopathy- Pre and post Anti VEGF treatment

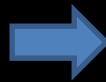
Macula OCT-R, 3 μ m above the ILM

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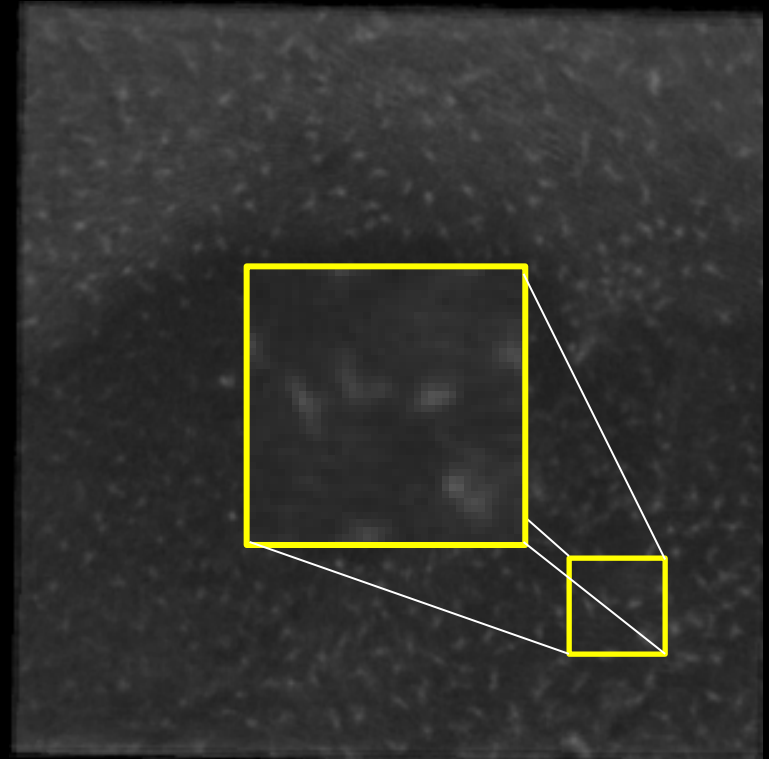
Pre Treatment



2 weeks after



Post Treatment

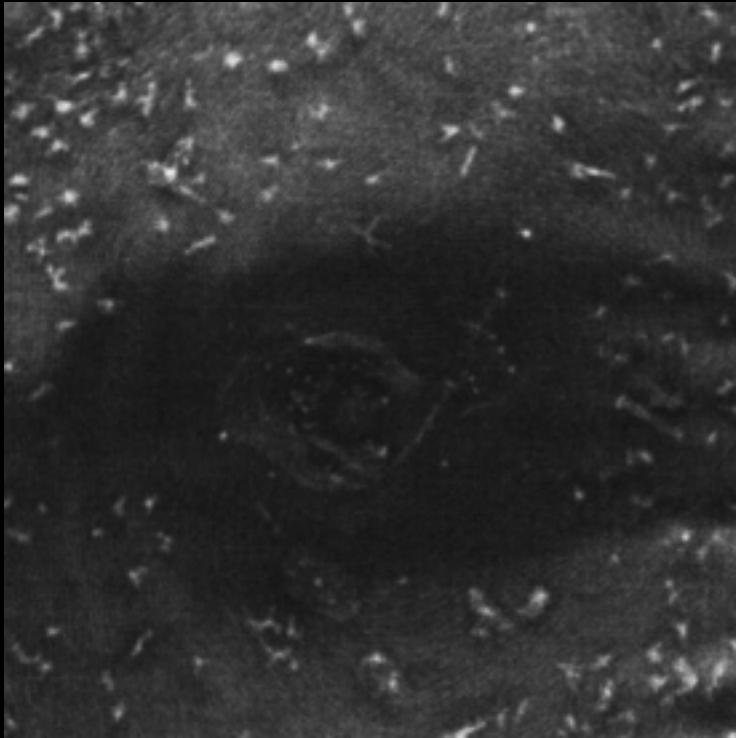


Diabetic Retinopathy- Pre and post Anti VEGF treatment

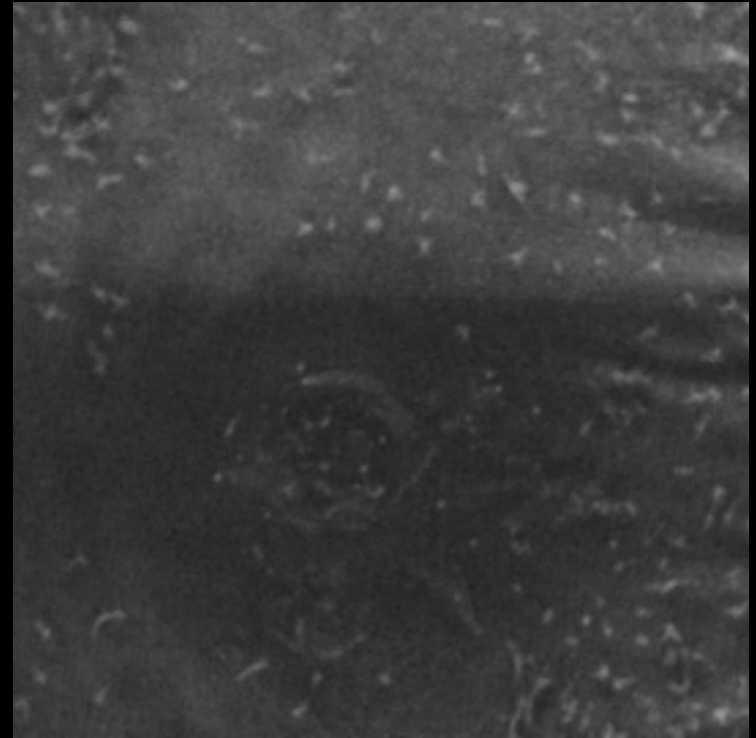
Macula OCT-R, 3 μ m above the ILM

Case 2

Pre Treatment



Post Treatment



2 weeks after

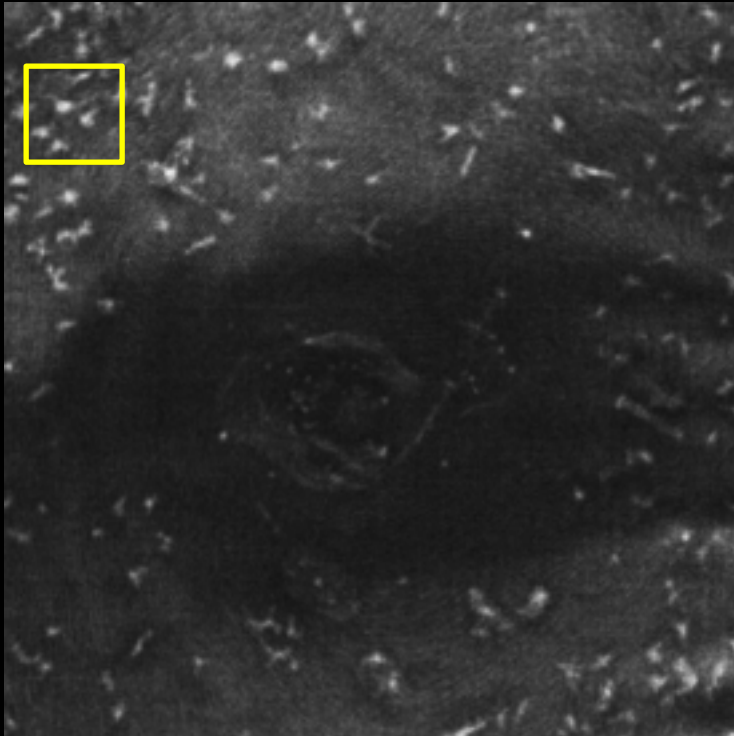


Diabetic Retinopathy- Pre and post Anti VEGF treatment

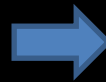
Macula OCT-R, 3 μ m above the ILM

Case 2

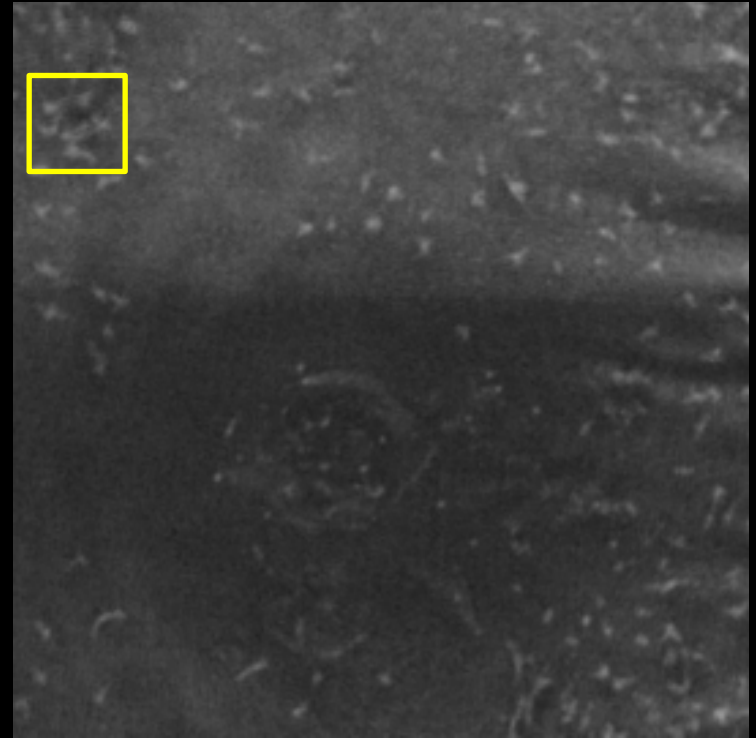
Pre Treatment



2 weeks after



Post Treatment

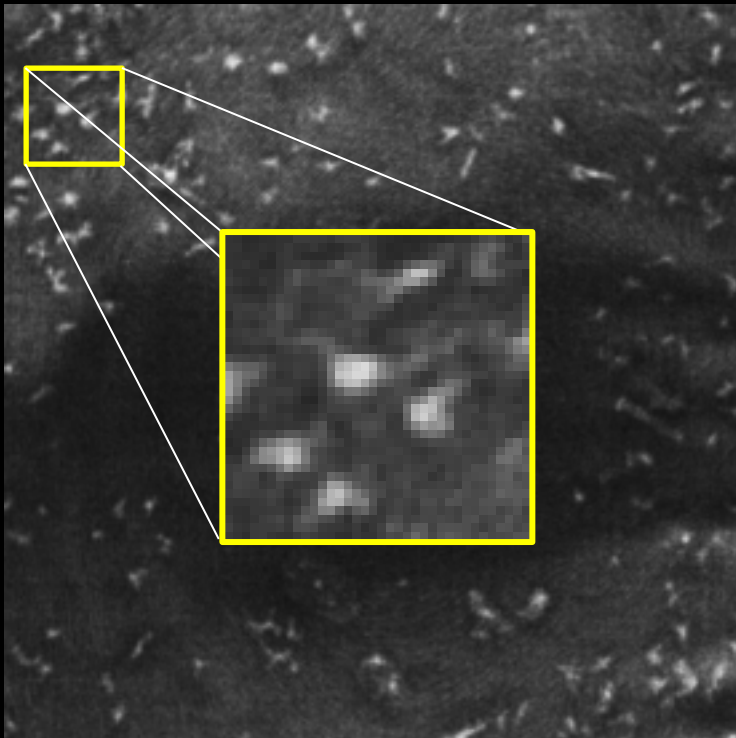


Diabetic Retinopathy- Pre and post Anti VEGF treatment

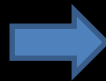
Macula OCT-R, 3 μ m above the ILM

Case 2

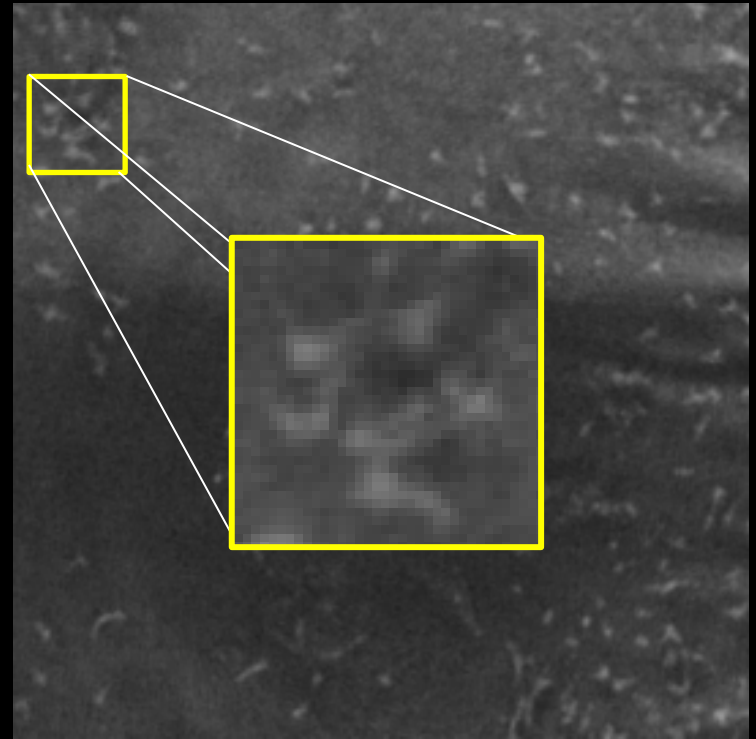
Pre Treatment



2 weeks after



Post Treatment



Results

- In controls, macrophages-like cells were not generally seen at the fovea. However, when present, the cells had a slender, star-like appearance and were sparsely distributed along the periphery of the macula.
- In diabetic eyes, in contrast, macrophages-like cells were consistently seen at increased densities at the macula and fovea. Cellular morphology varied from a spindle- or star-like configuration to amoeboid or round morphology and appeared bigger and brighter than in controls.
- Post injection images, showed changes in distribution and morphology of these cells.

Limitations

- Exact identity of these cells is still in question, currently based upon location and size, since we have no imaging markers .
- Limited sample size of population studied.
- 10 scan acquisition is clinically challenging for some patients.
- Accurate identification and characterization of these cells is not yet precise.

Conclusions

- Clinical OCT is capable of Imaging macrophage-like cells in eyes of patients with diabetic retinopathy.
- Visualizing these cells on macular OCT scans of diabetic patients could alert clinicians as an early sign of inflammation and impending retinal damage, making them useful early biomarkers of diabetic disease.
- Macrophage presence on the fovea of diabetic patients could prove useful for measuring response to treatment and ultimately serve as a guide for better management and prognosis
- Further clinical exploration will be needed to characterize their clinical significance and their relationship with extent and severity of retinal injury.
- Development of automated software and imaging protocols may have clinical value.

References

- Chen, X., Zhou, H., Gong, Y. *et al.* Early spatiotemporal characterization of microglial activation in the retinas of rats with streptozotocin-induced diabetes. *Graefes Arch Clin Exp Ophthalmol* **253**, 519–525 (2015). <https://doi-org.eresources.mssm.edu/10.1007/s00417-014-2727-y>
- Couturier A, Bousquet E, Zhao M, Naud MC, Klein C, Jonet L, Tadayoni R, de Kozak Y, Behar-Cohen F. Anti-vascular endothelial growth factor acts on retinal microglia/macrophage activation in a rat model of ocular inflammation. *Mol Vis.* 2014 Jun 23;20:908-20. PMID: 24966662; PMCID: PMC4067232.
- Kurokawa, K., Crowell, J. A., Zhang, F., & Miller, D. T. (2020). Suite of methods for assessing inner retinal temporal dynamics across spatial and temporal scales in the living human eye. *Neurophotonics*, 7(1), 015013 <https://doi.org/10.1117/1.NPh.7.1.015013>
- Maria V. Castanos, Davis B. Zhou, Rachel E. Linderman, Reilly Allison, Tatyana Milman, Joseph Carroll, Justin Migacz, Richard B. Rosen, Toco Y.P. Chui; Imaging of Macrophage-Like Cells in Living Human Retina Using Clinical OCT. *Invest. Ophthalmol. Vis. Sci.* 2020;61(6):48. doi: <https://doi.org/10.1167/iovs.61.6.48>.
- Liu Z, Kurokawa K, Zhang F, Lee JJ, Miller DT. Imaging and quantifying ganglion cells and other transparent neurons in the living human retina. *Proc Natl Acad Sci USA.* 2017; 114: 12803–12808.

Thanks!

