

Correlation of Retinal Thickness and Perfusion Metrics with Renal Function in Sickle Cell Retinopathy Using Optical Coherence Tomography (OCT) and OCT-Angiography



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Financial Disclosures

I have no relevant financial disclosures

My Role In This Research

- ☑ Conception and design of the work/project
- ☑ Acquisition of data
- ☑ Analysis and interpretation of data
- ☑ Creation and/or critical review of the presentation

Sickle Cell Disease

- The most common molecular genetic disease
 - Mutation in beta globin gene of hemoglobin
 - Associated with African (and Hispanic) ancestry
- Mutation confers genetic advantage:
 - Protects against *Plasmodium falciparum* malaria
 - Example of balanced polymorphism
 - Homozygote sickle poor survival from sickle cell disease
 - Normal Hgb poor survival from prevalent malaria
 - Sickle Hgb + normal Hgb = better survival

Sickle Cell Disease

- Over 100,000 affected in the United States¹
 - About 1:13 African-Americans born with sickle cell trait
 - About 1:365 African-Americans born with sickle cell disease
 - About 1:16,300 Hispanic-Americans born with sickle cell trait
- Sickle cell disease is deadly:²
 - 11% have clinically apparent strokes by age 20
 - 24% have clinically apparent strokes by age 45

¹Hassel KL. Population estimates of sickle cell disease in the U.S. Am J Prev Med 2010;38(4S):S512-S521.

²Ohene-Frempong K, Weiner SJ, Sleeper LA, et. al. Cerebrovascular accidents in sickle cell disease: Rates and risk factors. Blood 1998;91(1):288-294.

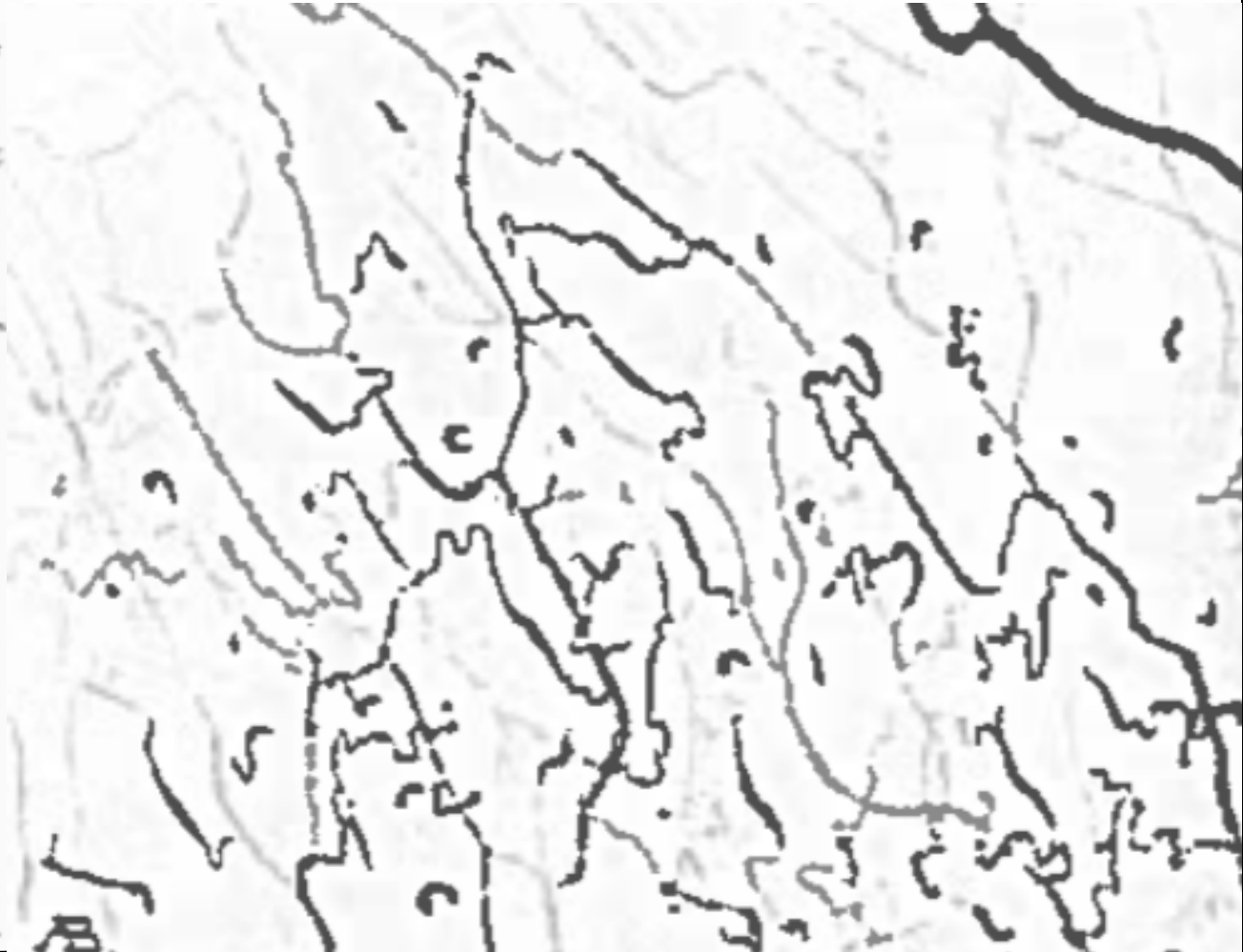
The Conjunctival Sign of Sickle-Cell Disease

DAVID PATON, M.D., Baltimore

ARCHIVES OF OPHTHALMOLOGY Vol. 66, July, 1961

Results of Slit-Lamp Examination of Conjunctival Vessels in 116 Black Patients

Hematology Clinic Patients Diagnosis Unknown	Capillaries *		?	Referred Patients, Diagnosis Known or Suspected	Capillaries		?
	-	+			-	+	
Hgb Type	-	+	?	-	+	?	
A (normal)	61			2			
S-S		19			7		
S-C		4			4	2	
S-A	8		2	2			
S-F	1						
S-Thal	1						
C-A	4						
F-A			1				



Ocular Findings and Sickle Cell Burden

The Conjunctival Sign in Sickle Cell Anemia

A Relationship With Irreversibly Sickled Cells

Graham R. Serjeant, MB, MRCP; Beryl E. Serjeant, FIMLT; and Patrick I. Condon, MCh, FRCS

**Irreversibly Sickled Cell (ISC) Counts
By Degree of Conjunctival Vessel Abnormality**

Grade of Conjunctival Vessel Abnormality	No. of Patients	Male	Female	Mean Age (yr)	ISC (Mean \pm SD)
0	2	2	0	11.5	1.0 \pm 1.4
1	12	4	8	29.2	8.6 \pm 4.9
2	14	9	5	19.4	10.6 \pm 4.4
3	21	7	14	24.7	12.3 \pm 5.5
4	17	8	9	24.3	18.5 \pm 6.4

OCT-Angiography

- Non-invasive, dye-less angiography
 - Superficial, intermediate, and deep plexus visualization
- Clinical Applications:
 - Foveal avascular zone (FAZ) visualization
 - Non-perfusion
 - Microvascular changes and neovascularization
- **Quantitative analysis of retinal microvasculature:**
 - *FAZ area*
 - *vascular density and vessel complexity*

OCT-Angiography and Systemic Diseases

- Correlation of microvascular metrics with systemic disease
 - Vascular density, non-perfused area, fractals
 - Potential use of OCT-Angiography (OCTA) as a biomarker

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 - Myocardial Infarction

The EYE-MI Pilot Study: A Prospective Acute Coronary Syndrome Cohort Evaluated With Retinal Optical Coherence Tomography Angiography

Louis Arnould,¹⁻³ Charles Guenancia,^{4,5} Arthur Azemar,⁴ Guillaume Alan,⁴ Stéphane Pitois,⁴ Florence Bichat,⁴ Marianne Zeller,⁴ Pierre-Henry Gabrielle,^{1,3} Alain M. Bron,^{1,3} Catherine Creuzot-Garcher,^{1,3} and Yves Cottin^{4,5}

OCT-Angiography and Systemic Diseases

- Correlation of microvascular metrics with systemic disease
 - Vascular density, non-perfused area, fractals
 - Potential use of OCT-Angiography (OCTA) as a biomarker
 - Myocardial Infarction
 - Alzheimer's Disease

Evaluation of optical coherence tomography
angiographic findings in Alzheimer's type dementia

Mehmet Bulut,¹ Fatma Kurtuluş,² Onursal Gözkaya,³ Muhammet Kazım Erol,¹
Ayşe Cengiz,¹ Melih Akıdan,¹ Aylin Yaman²

OCT-Angiography and Systemic Diseases

- Correlation of microvascular metrics with systemic disease
 - Vascular density, non-perfused area, fractals
 - Potential use of OCT-Angiography (OCTA) as a biomarker
 - Myocardial Infarction
 - Alzheimer's Disease
 - Sickle Cell Disease

Study Purpose

- To evaluate retinal thickness and perfusion metrics using OCT and OCT Angiography (OCTA) in sickle cell retinopathy and determine their relationship to renal function
- *To evaluate retinal microvascular metrics using OCTA in sickle cell retinopathy in relation to visual acuity*

Methods

- 79 eyes in 44 patients with sickle cell disease
- OCT and OCT-angiography performed using Zeiss Cirrus HD-OCT 5000 (Carl Zeiss Meditec, Inc., Dublin CA, USA)
 - OCT metrics included average cube thickness and volume, average ganglion cell layer (GCL) thickness, and central subfield thickness (CST) per ETDRS grid using standard 512x128 scans
 - ImageJ (Bethesda, MD) post-capture processing to determine foveal avascular zone area (FAZ), vessel density (VD), and vessel complexity (VC) at both the superficial (sFAZ, sVD, sVC) and deep (dFAZ, dVD, dVC) plexuses using 3x3 mm scans
- Statistical correlation of OCT and OCTA metrics with renal function (serum creatinine) and visual acuity (VA)

Results

Patient Demographics

- 44 African-American patients were included:
 - Mean Age = 30 years (median: 27, range: 15-65)
 - 19 Males and 25 females
- Sickle Cell Type:
 - Sickle Cell **Trait = 0**
 - Sickle Cell **SS = 23**
 - Sickle Cell **SC = 17**
 - Sickle Cell **S-thal = 4**

Results

Medical History

- Diabetes mellitus = 2
- Hypertension = 10
- Stroke = 10
- Avascular necrosis = 20
- History of crisis year prior to OCTA = 23
 - Mean number of incidents: 6.2 (median: 3, range: 1-26)

Results

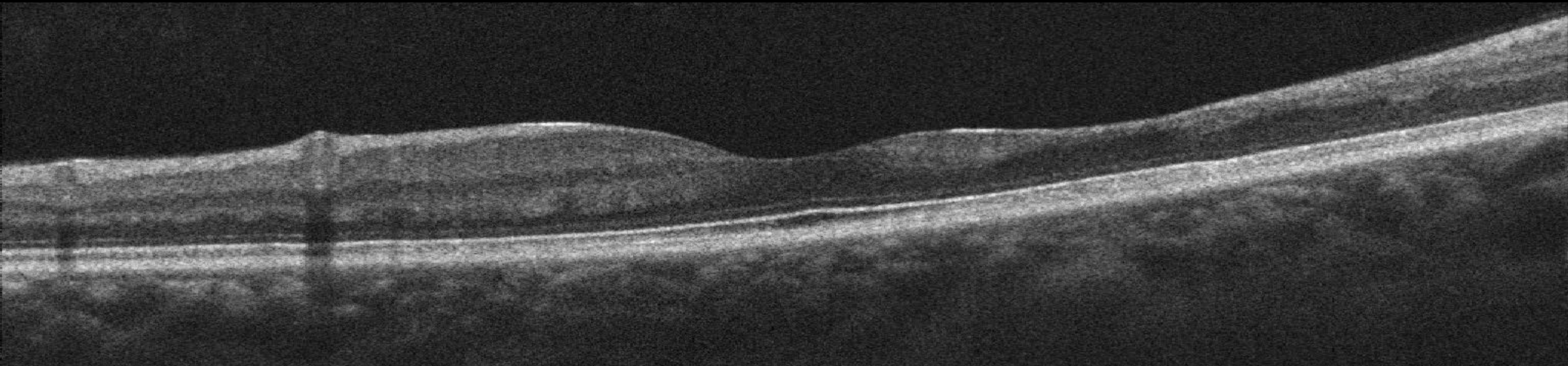
Clinical Features

- Visual Acuity:
 - Mean logMAR = 0.1 (median = 0, range: 0-1)
 - 20/20 to 20/25 = 68 eyes (86%)
 - 20/30 to 20/40 = 9 eyes (12%)
 - 20/50 to 20/200 = 2 eyes (2%)
- Intraocular Pressure:
 - Mean IOP = 16mmHg (median: 16, range: 10-22)

Results

OCT Features

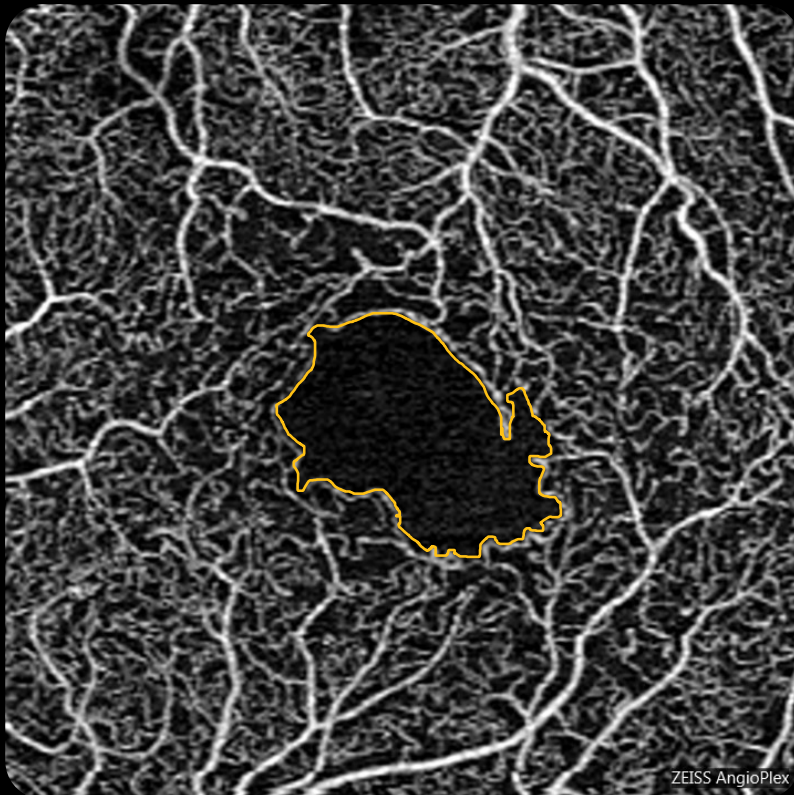
- Mean CST = 233 μm (median: 234, range: 154-299)
- Mean cube volume = 9.8 mm^3 (median: 9.9, range: 6.7-11.4)
- Mean cube thickness = 273 μm (median: 275, range: 186-318)
- Mean GCL thickness = 79 μm (median: 81, range: 12-106)



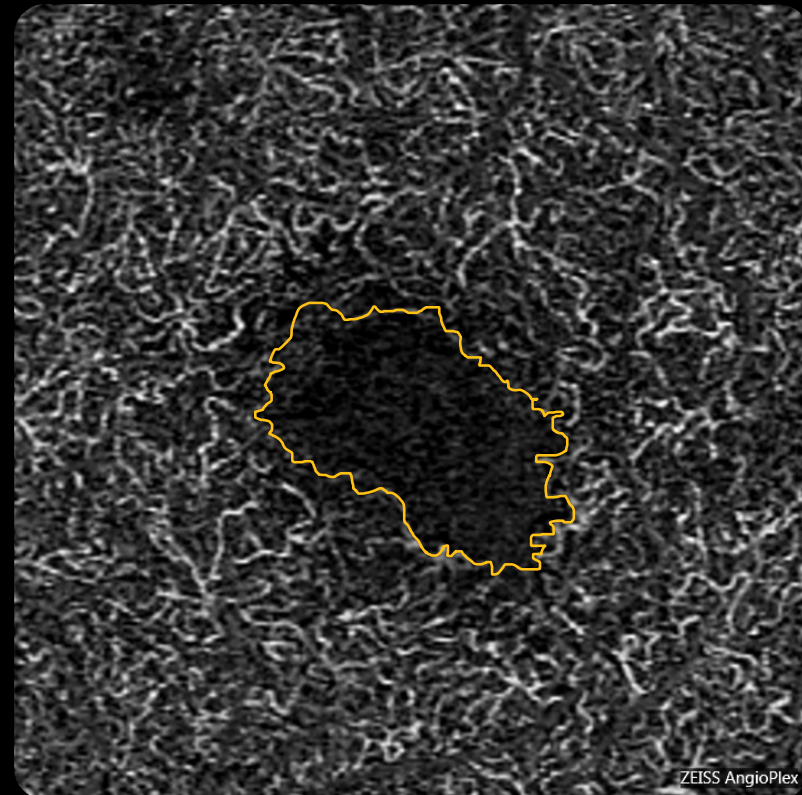
Results - OCTA Features

Mean FAZ area (median, range):

Superficial Plexus = 0.398mm^2
(0.408, 0.106-0.826)



Deep Plexus = 0.578mm^2 (0.566,
0.198-1.196)

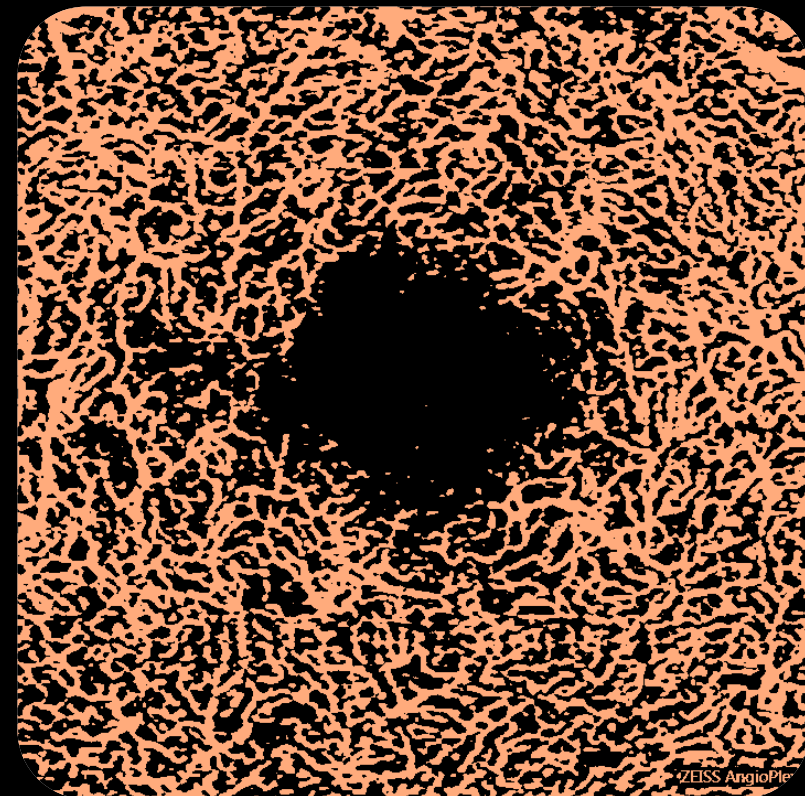
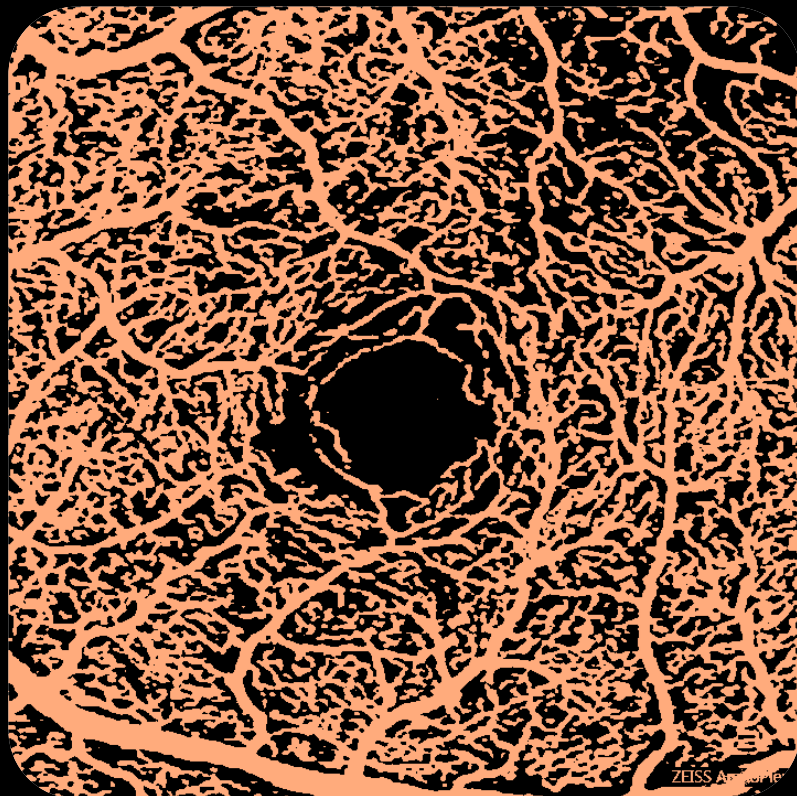


Results - OCTA Features

Mean Vessel Density (median, range):

Superficial Plexus = 51% (52,
24-60)

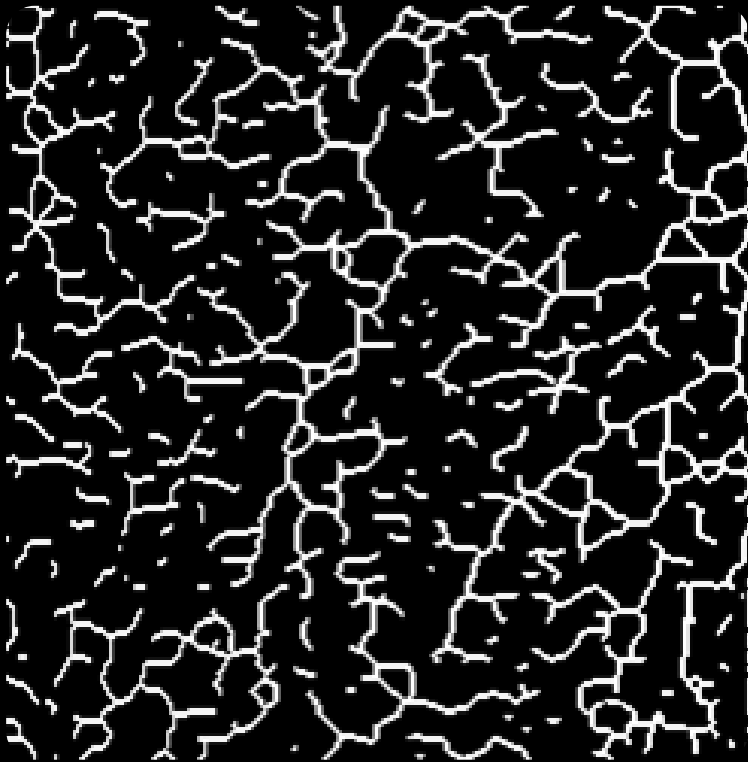
Deep Plexus = 47% (47, 37-53)



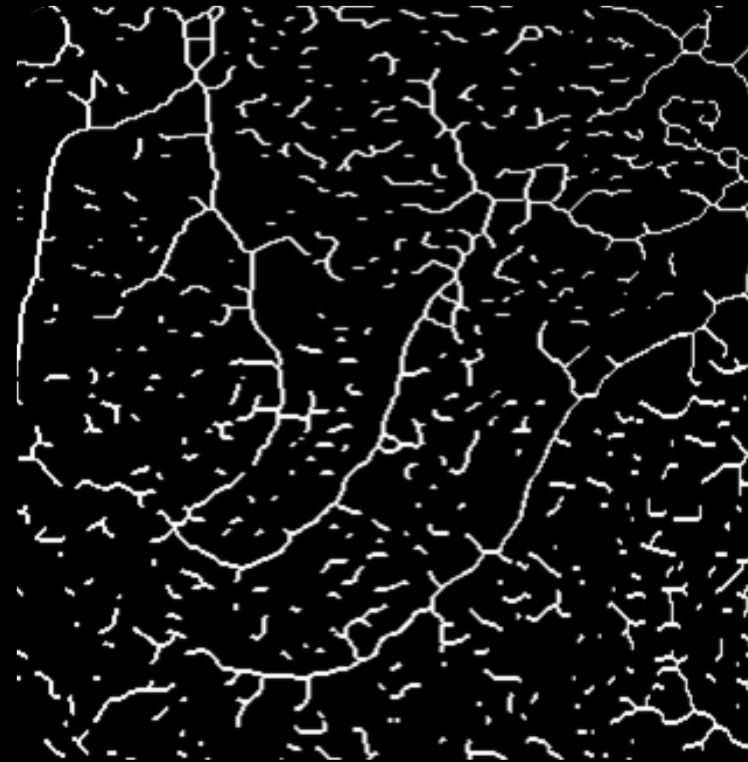
Results - OCTA Features

Mean Fractal Dimension (median, range):

Superficial Plexus = 1.772
(1.777, 1.643-1.796)



Deep Plexus = 1.773
(1.774, 1.726-1.801)



Results

Renal Function

GFR category	GFR (mL/min/1.732 m²)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

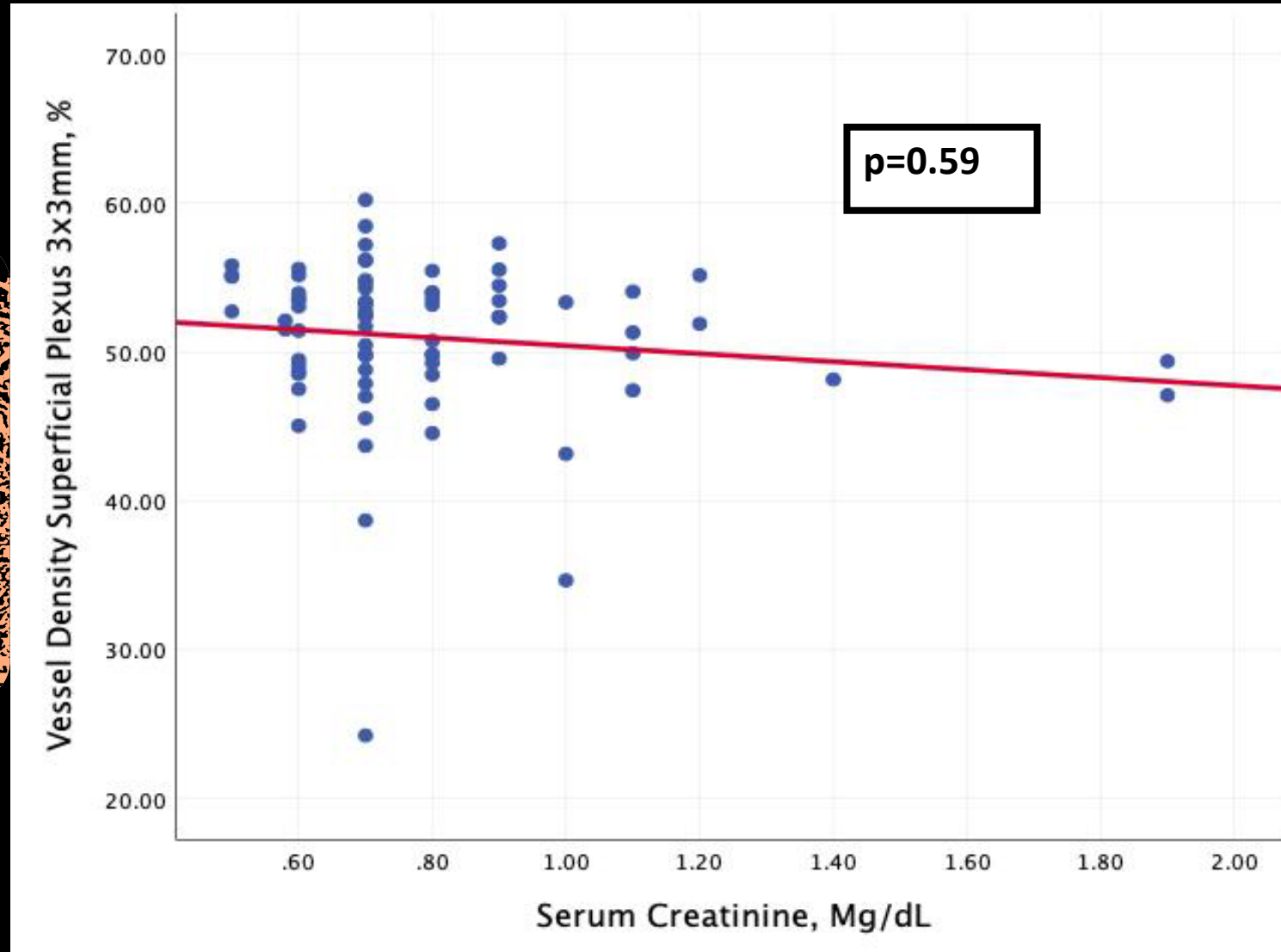
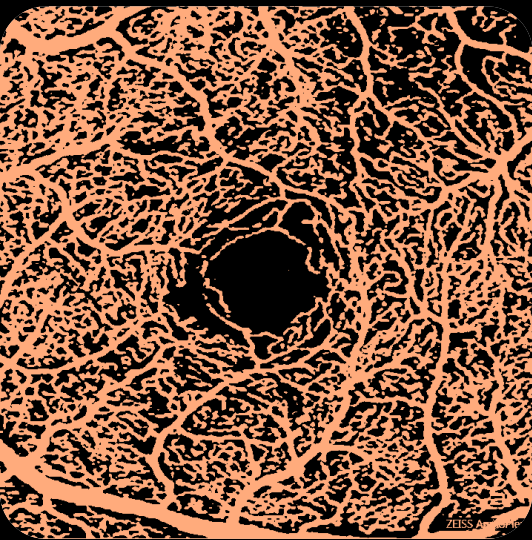
Results

Renal Function

- Estimated Glomerular Filtration Rate (eGFR):
 - G1/G2 (>59) = 71 (89%)
 - G3a (mild to moderately decreased) = 1 (1%)
 - G3b (moderately to severely decreased) = 1 (1%)
 - Not tested due to age <18 years = 6 (7%)
- Mean serum creatinine (median, range):
 - 0.79mg/dL (0.7, 0.5-1.9)

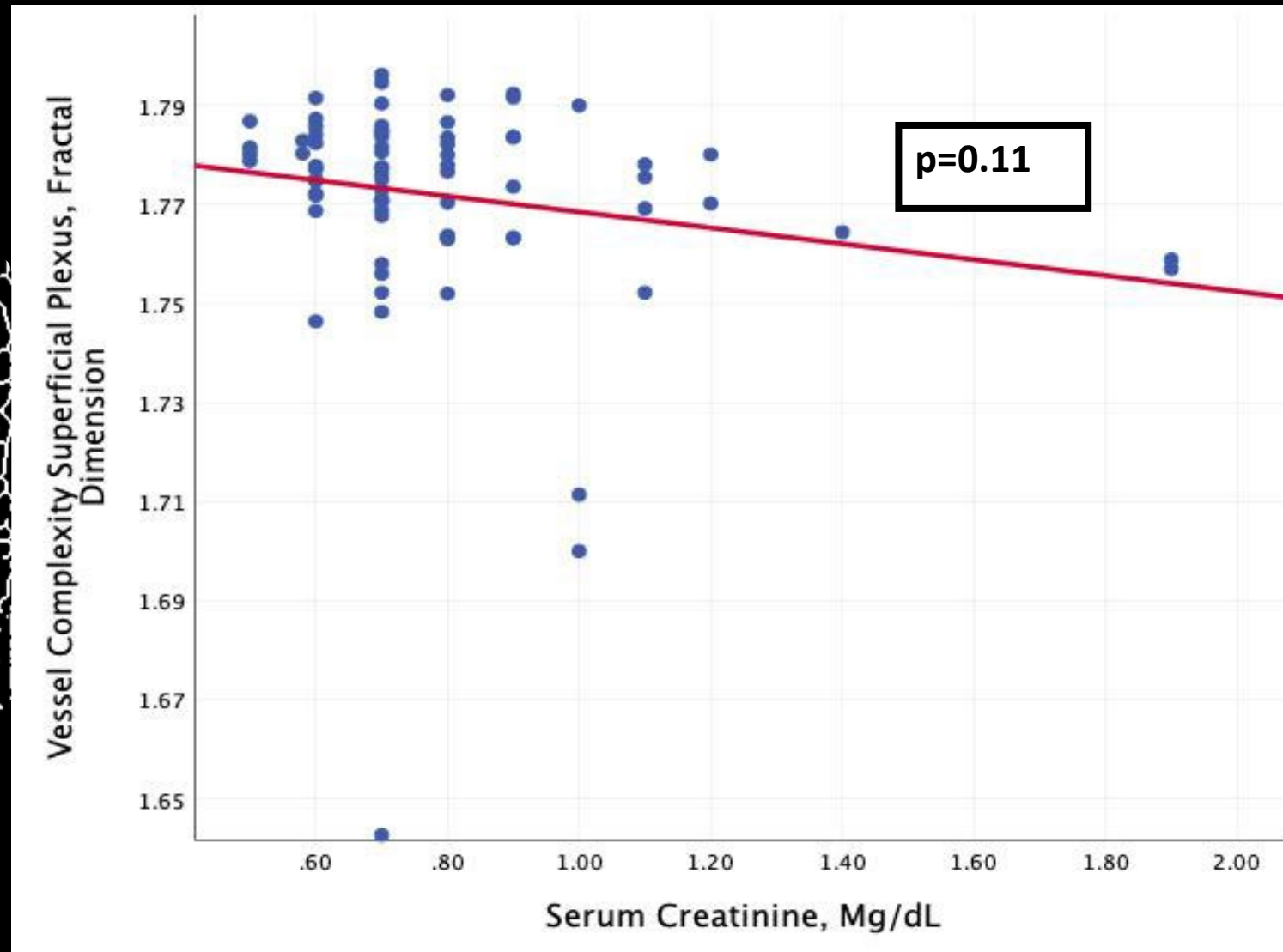
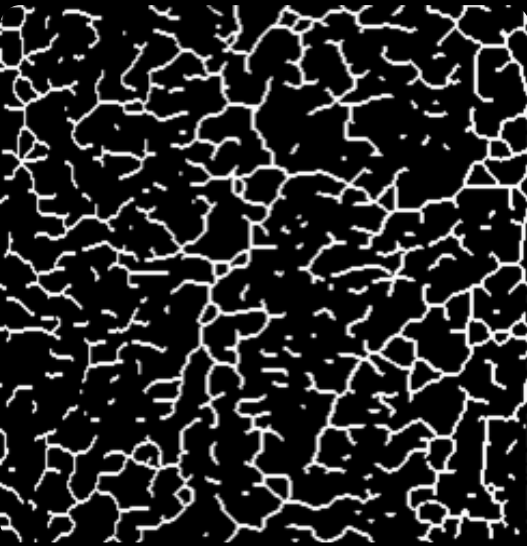
Results

Superficial Plexus VD – Renal Function Correlation



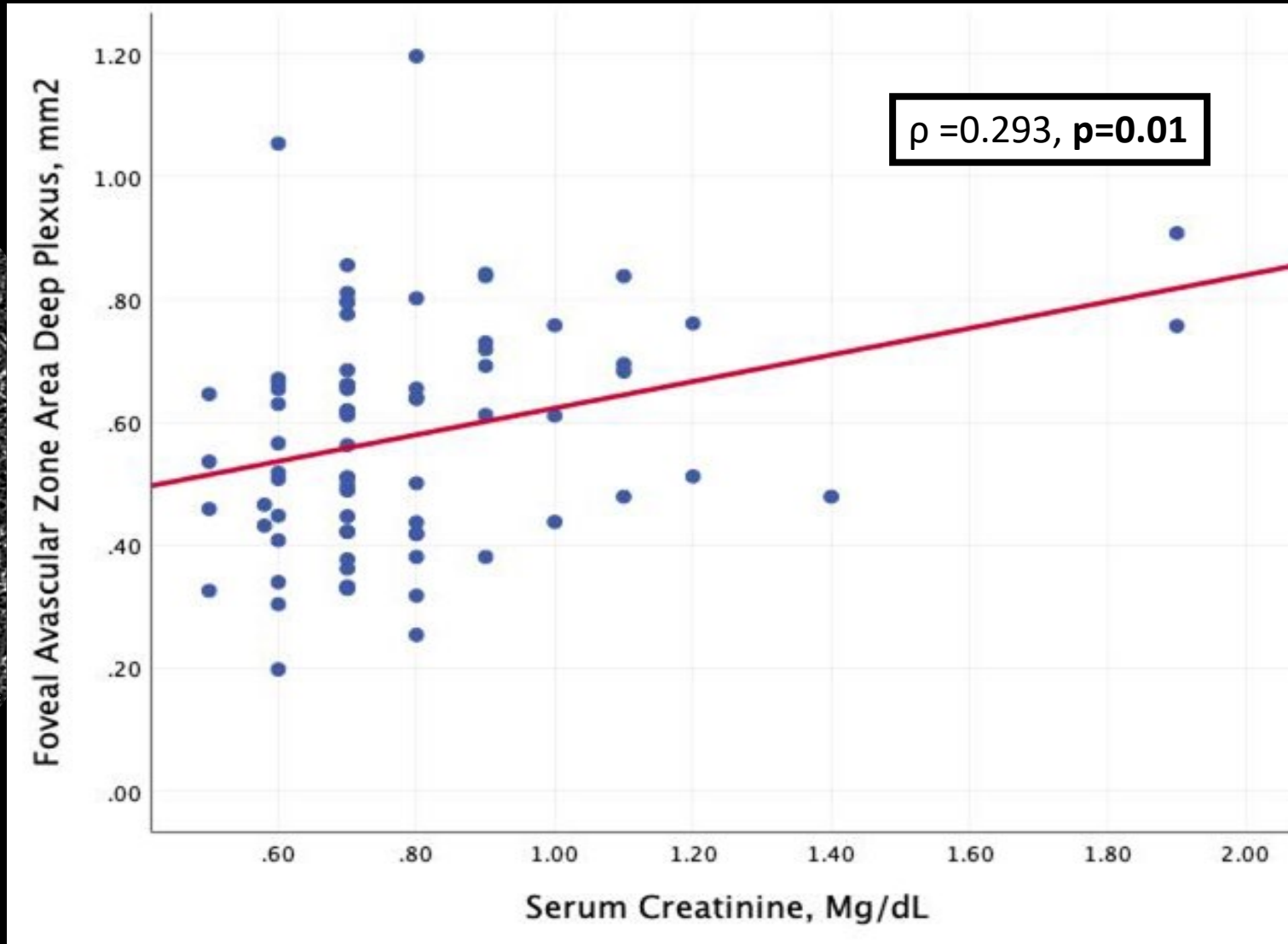
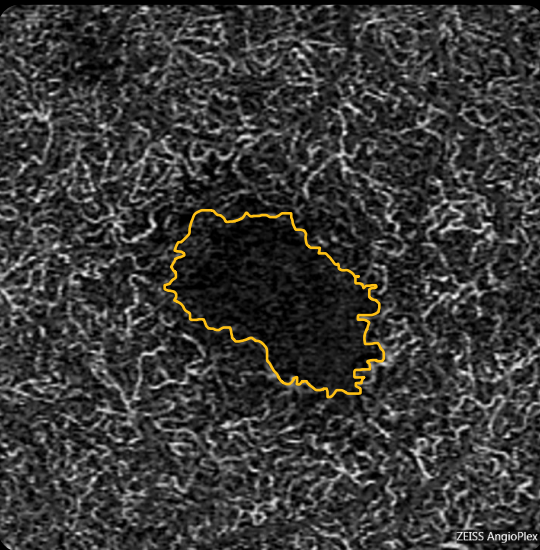
Results

Superficial Plexus FD – Renal Function Correlation



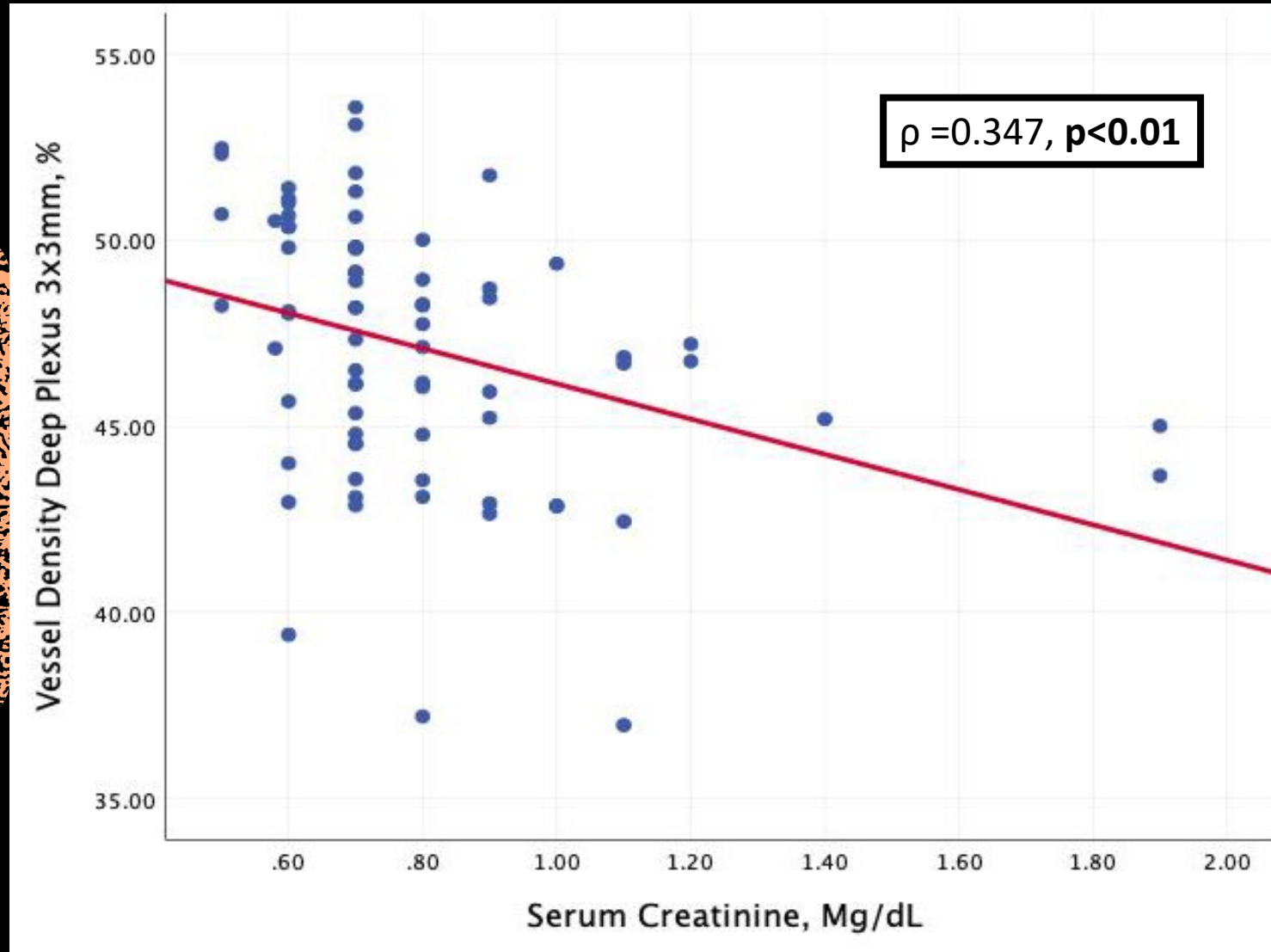
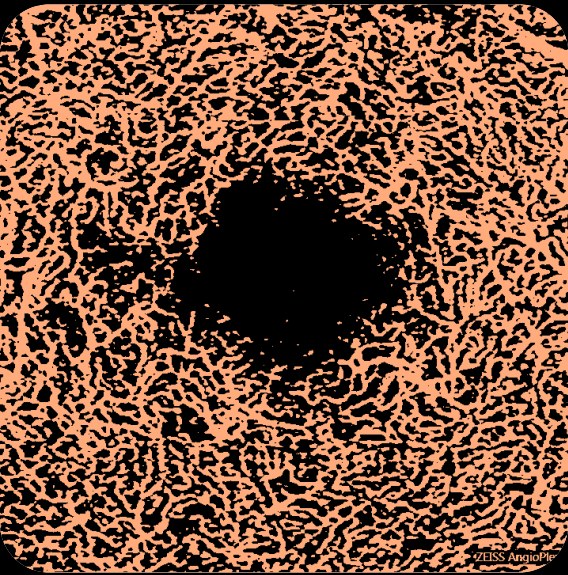
Results

Deep Plexus FAZ– Renal Function Correlation



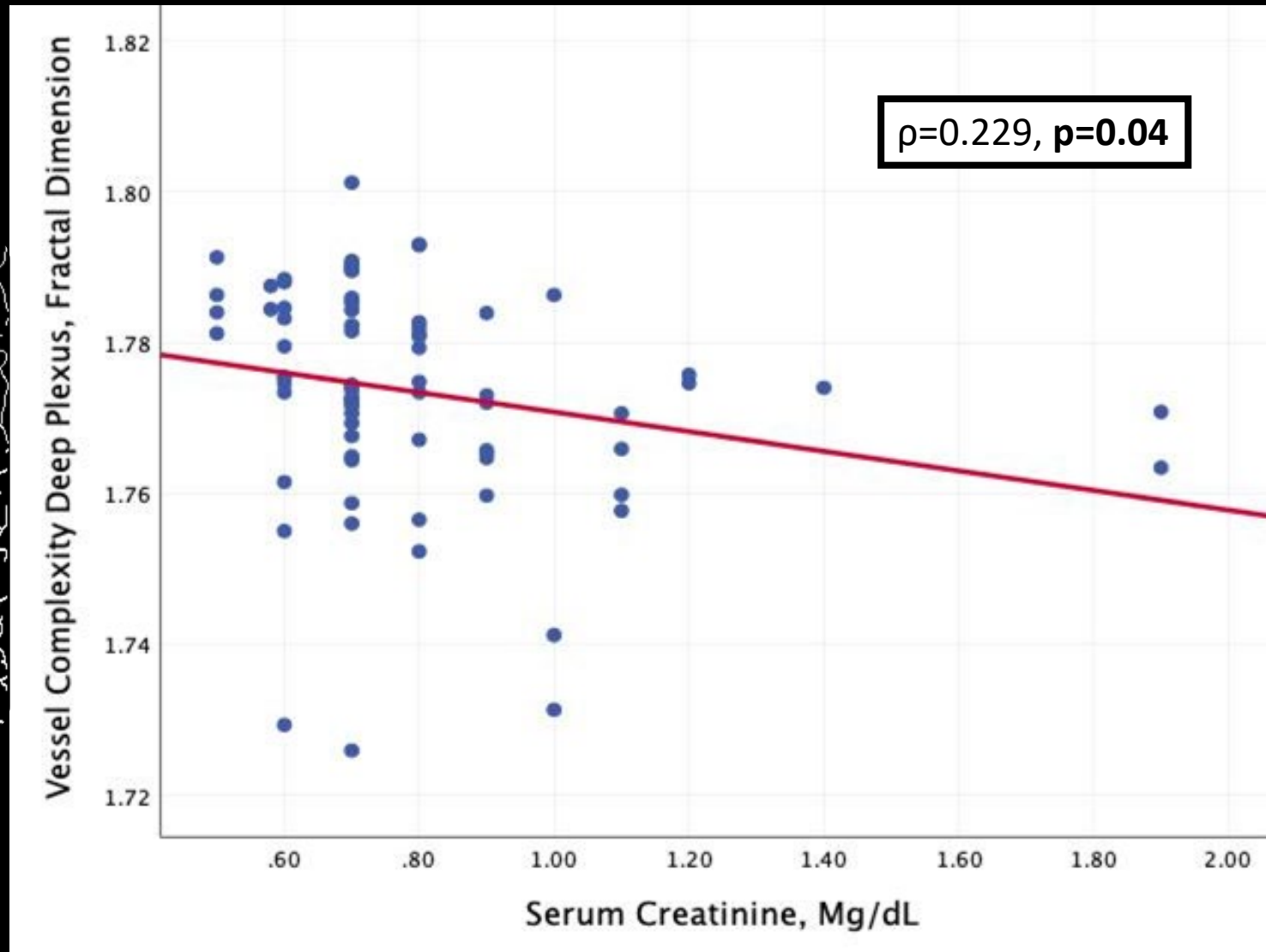
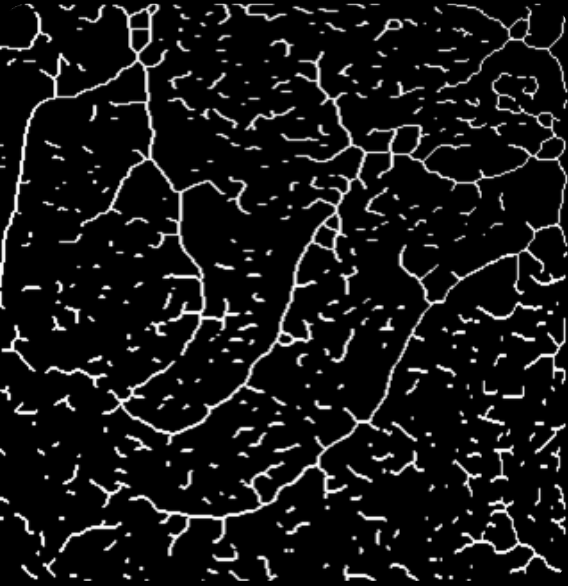
Results

Deep Plexus VD– Renal Function Correlation



Results

Deep Plexus FD – Renal Function Correlation



Results

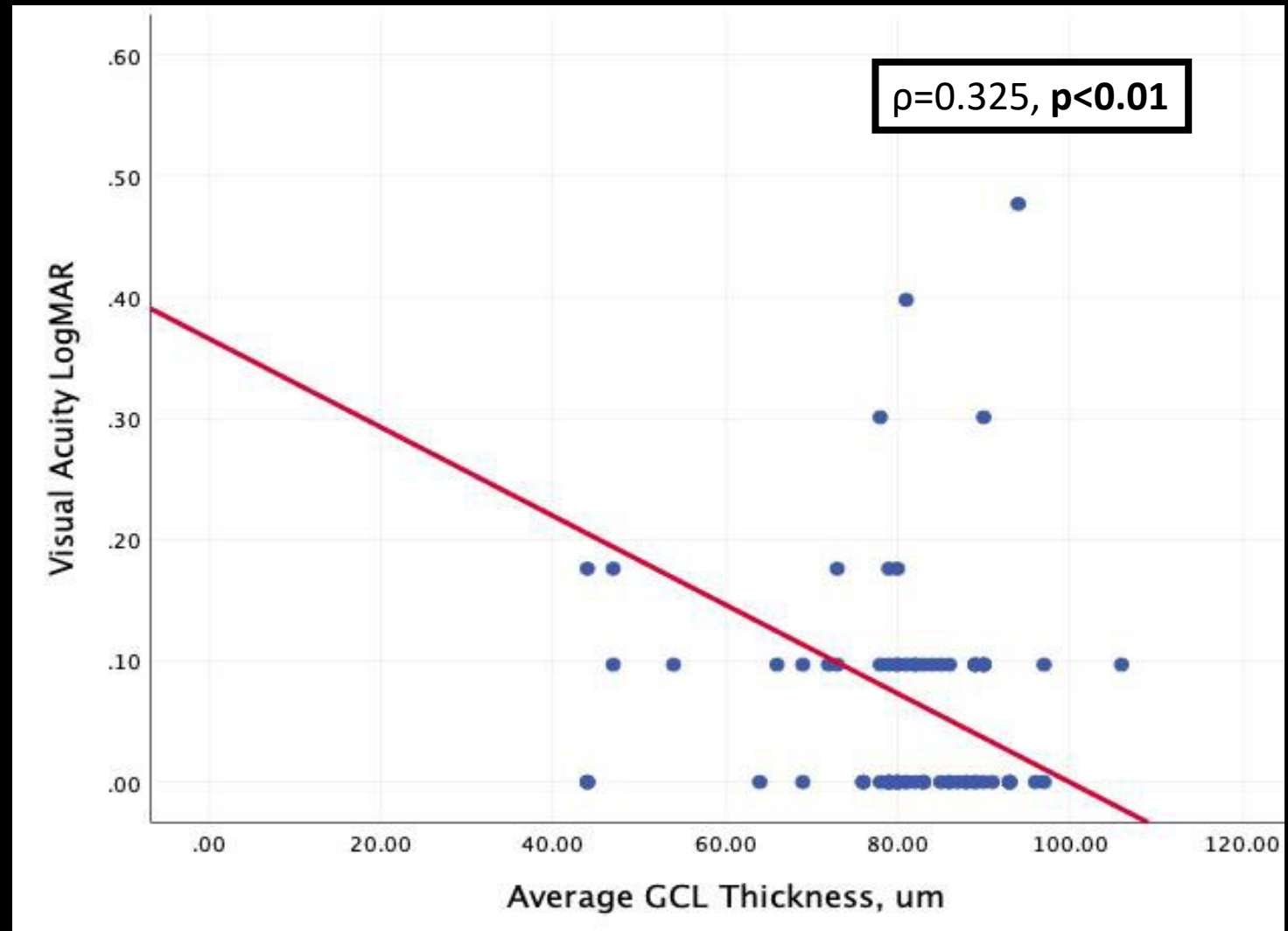
OCT

- no statistically significant correlation between serum biomarkers and any of the OCT metrics.

Results

OCT – LogMAR Vision Correlation

- **Superficial Plexus:**
 - **GCL average thickness and LogMAR.**



Results

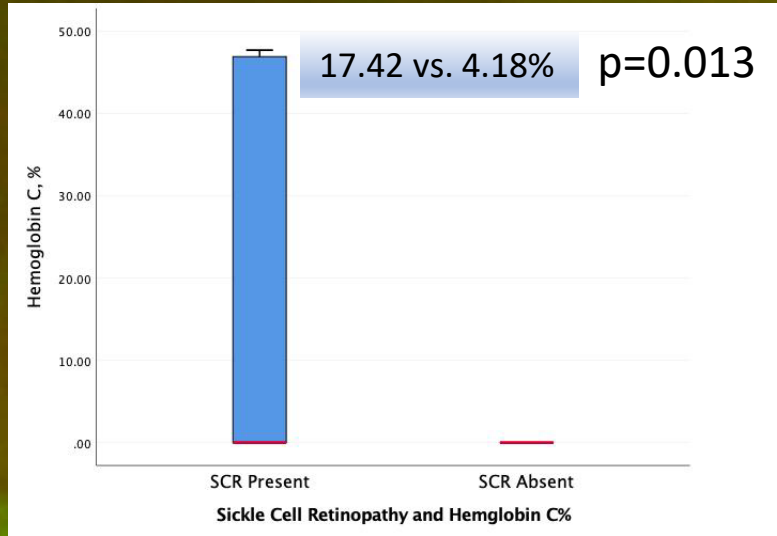
OCTA – LogMAR Vision Correlation

- **Superficial Plexus:**
 - **sFAZ and logMAR: $p < 0.01$**
 - **sVD and logMAR: $p < 0.01$**
 - **sVC and logMAR: $p < 0.01$**
- **Deep Plexus:**
 - dFAZ and logMAR: $p = 0.28$
 - dVD and logMAR: $p = 0.11$
 - dVC and logMAR: $p = 0.07$

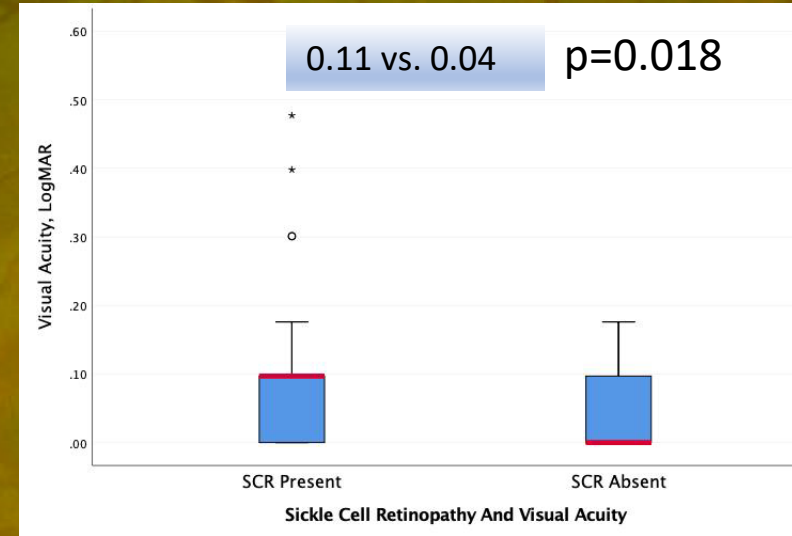


Subgroup Analysis Sickle Cell Retinopathy (SCR) Vs. No SCR

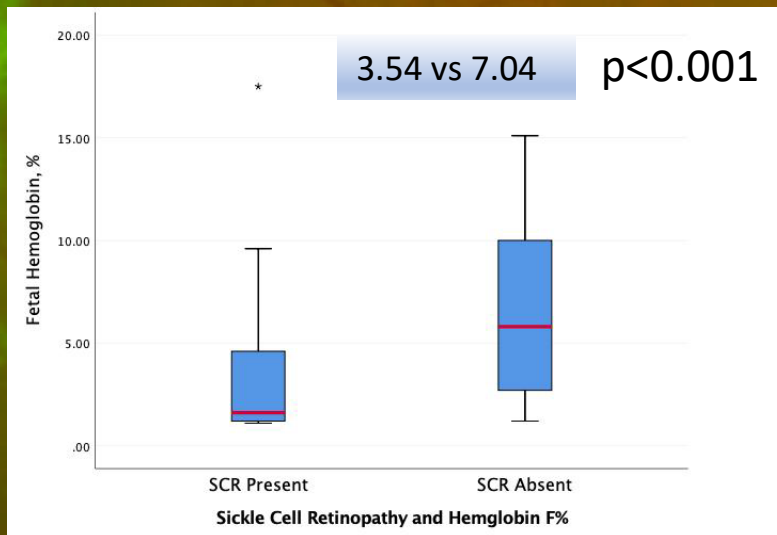
Hemoglobin C



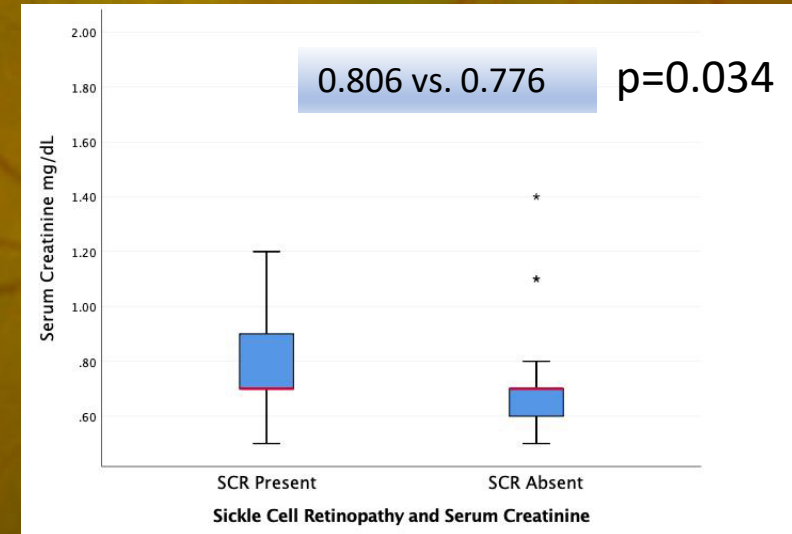
Visual Acuity



Fetal Hemoglobin



Serum Creatinine



Summary

- Correlation between retinal microvascular parameters and renal function in sickle cell disease
 - No correlation of sVD and sVC with serum creatinine
 - Correlation of sFAZ, dFAZ, dVD, and dVC with serum creatinine
- Correlation between logMAR visual acuity and sFAZ, sVD, and sVC but not with deep plexus parameters
- Patients with evidence of SCR demonstrated elevated Cr and HbS, and decreased HbF

Thank you for your kind attention