Imaging in Diabetic Retinopathy

OCT Angiography

Dawn Sim
Consultant Ophthalmologist
Moorfields Eye Hospital

2016

255 778 OCTs

Diabetic Eye Disease

Diabetic Macular Oedema

Sight-threatening

Diabetic Macular Ischaemia

Retinal blood vessels

Neovascularisation

Retinal imaging techniques used for:

Oedema

Ischaemia

Neovascularisation

1. Detection

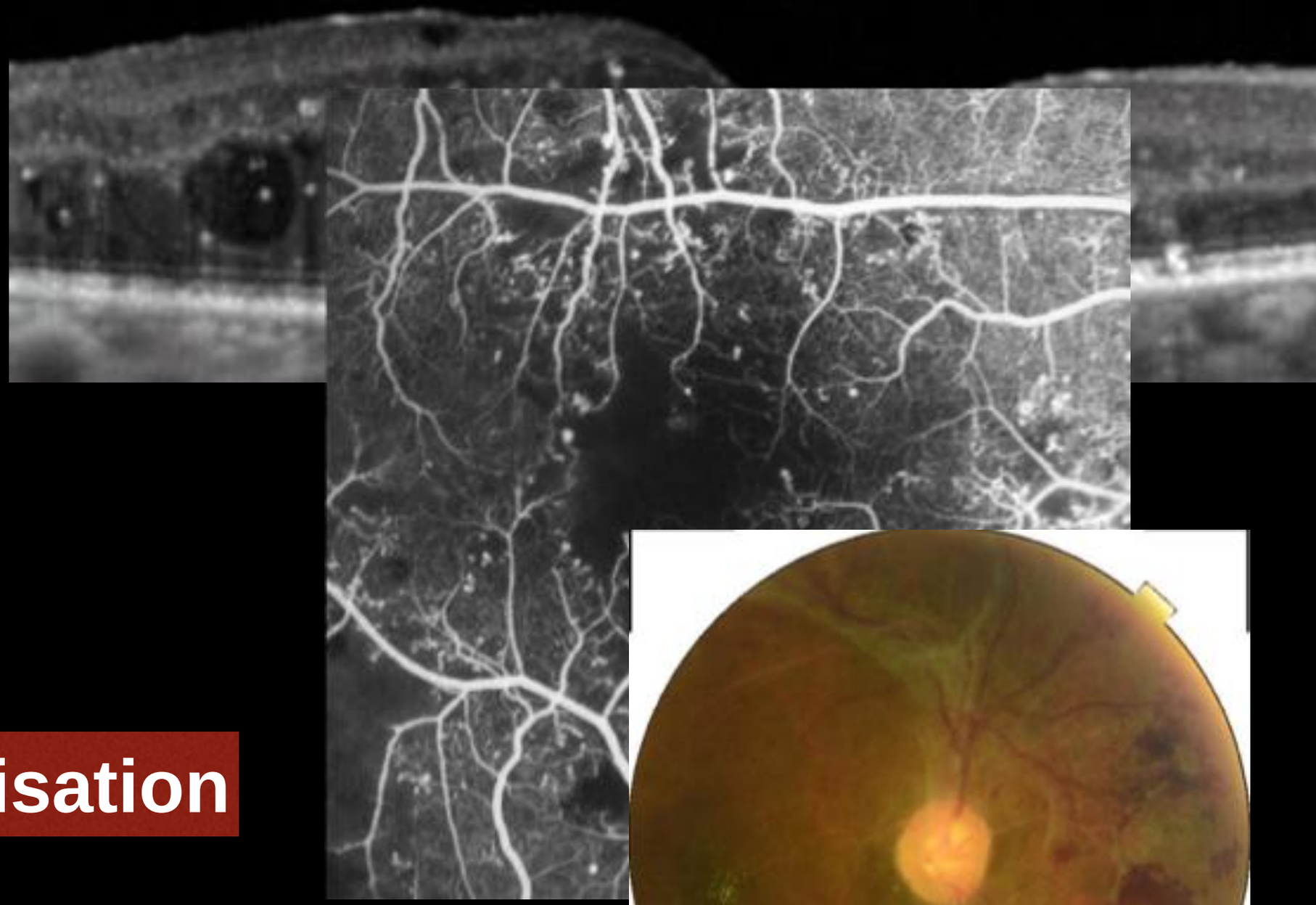
2. Monitoring

Well established imaging modalities

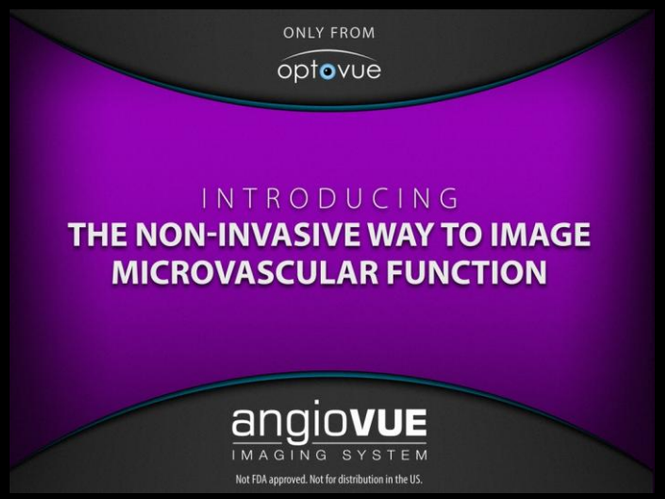
Oedema

Ischaemia

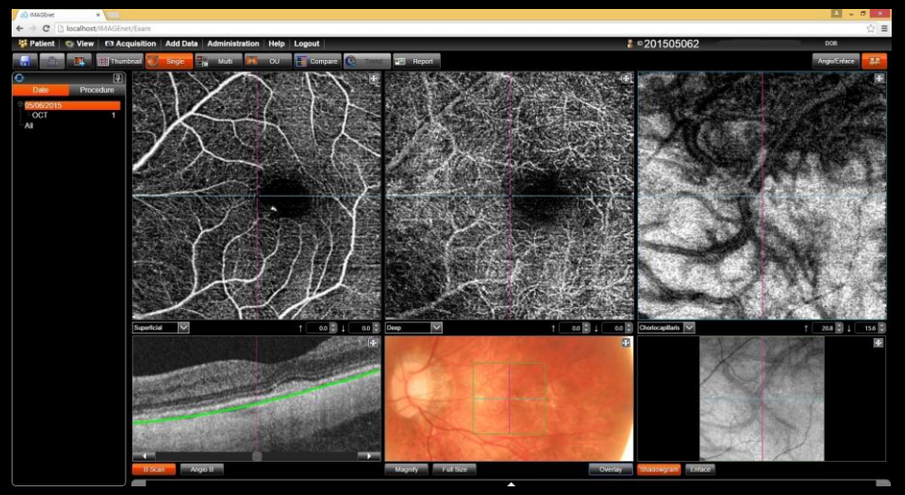
Neovascularisation



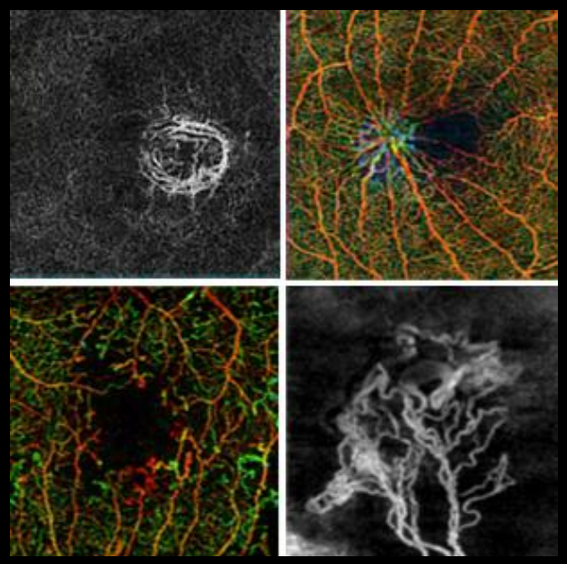
Multiple commercial systems



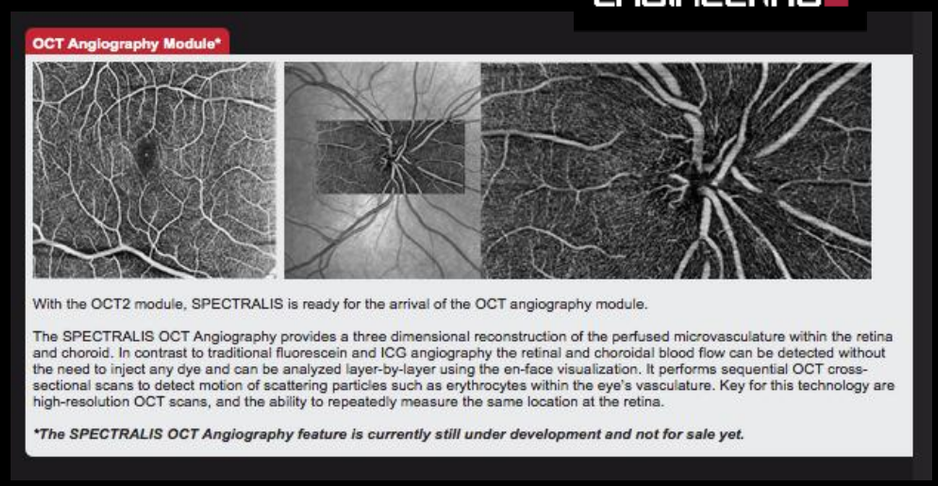
TOPCON



ZEISS



HEIDELBERG ENGINEERING



Pros…

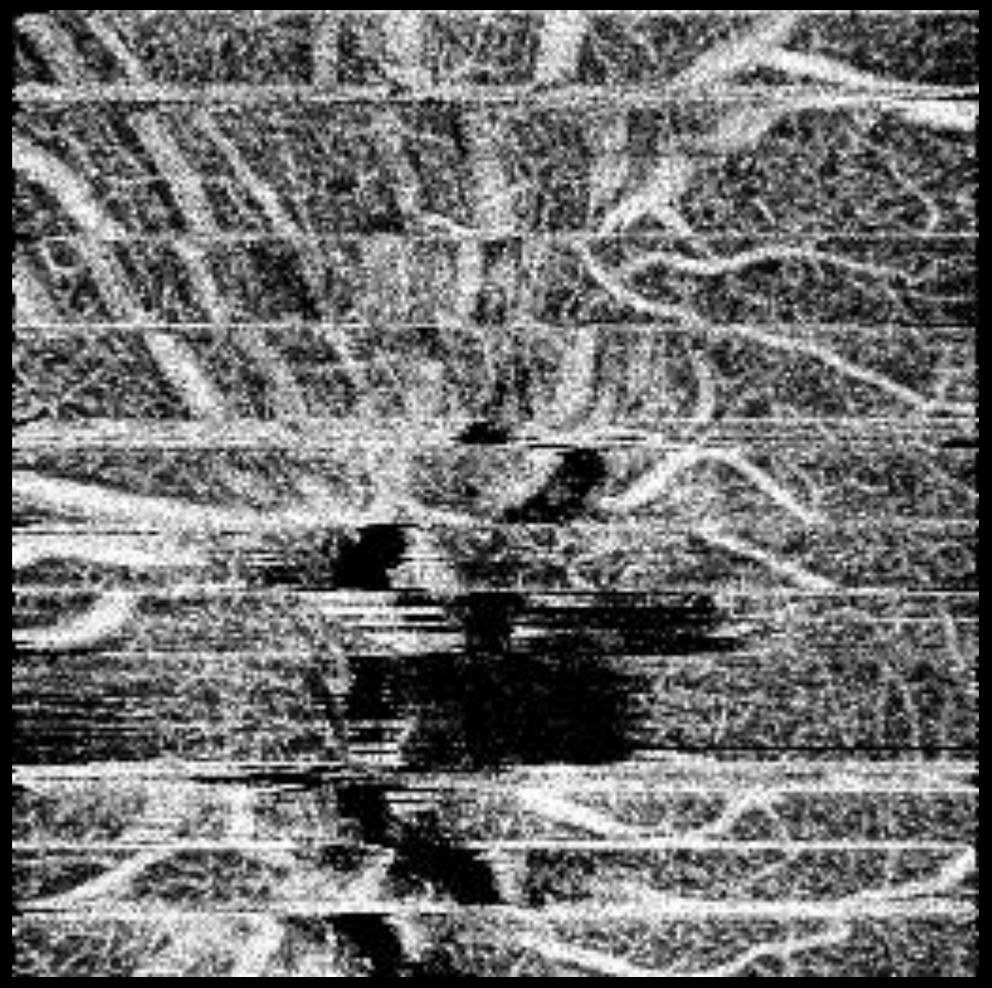
OCTA	FFA
Non invasive	Well established
Rapid acquisition	Widefield
Depth information	Less artefacts
Penetrates haem	Real flow information

Cons…

OCTA	FFA
Paucity of clinical validation	Invasive
Motion/Projection artifacts	Time consuming
Limited field of view	unpleasant

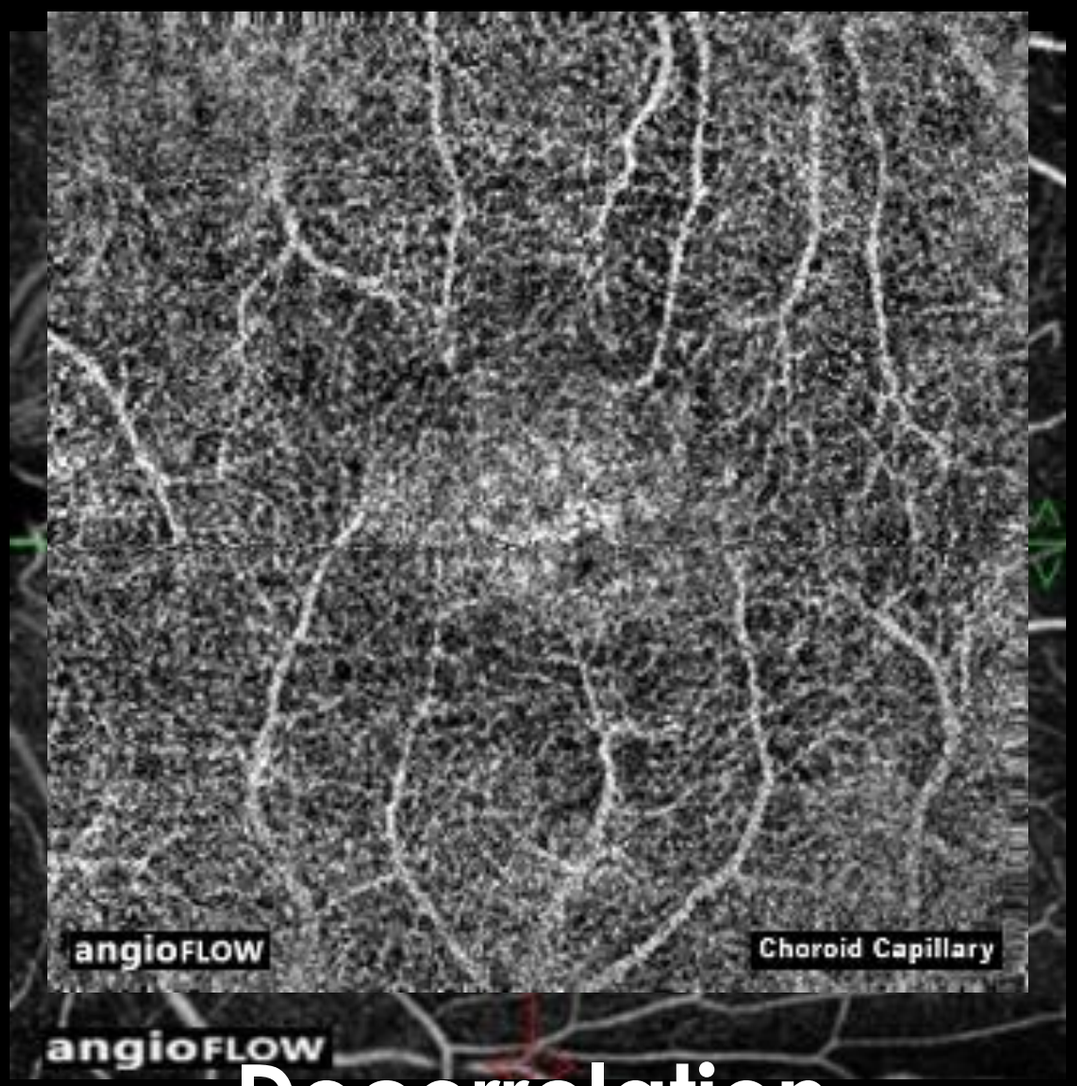
Motion Artifacts

Optovue



Topcon

Other artifacts



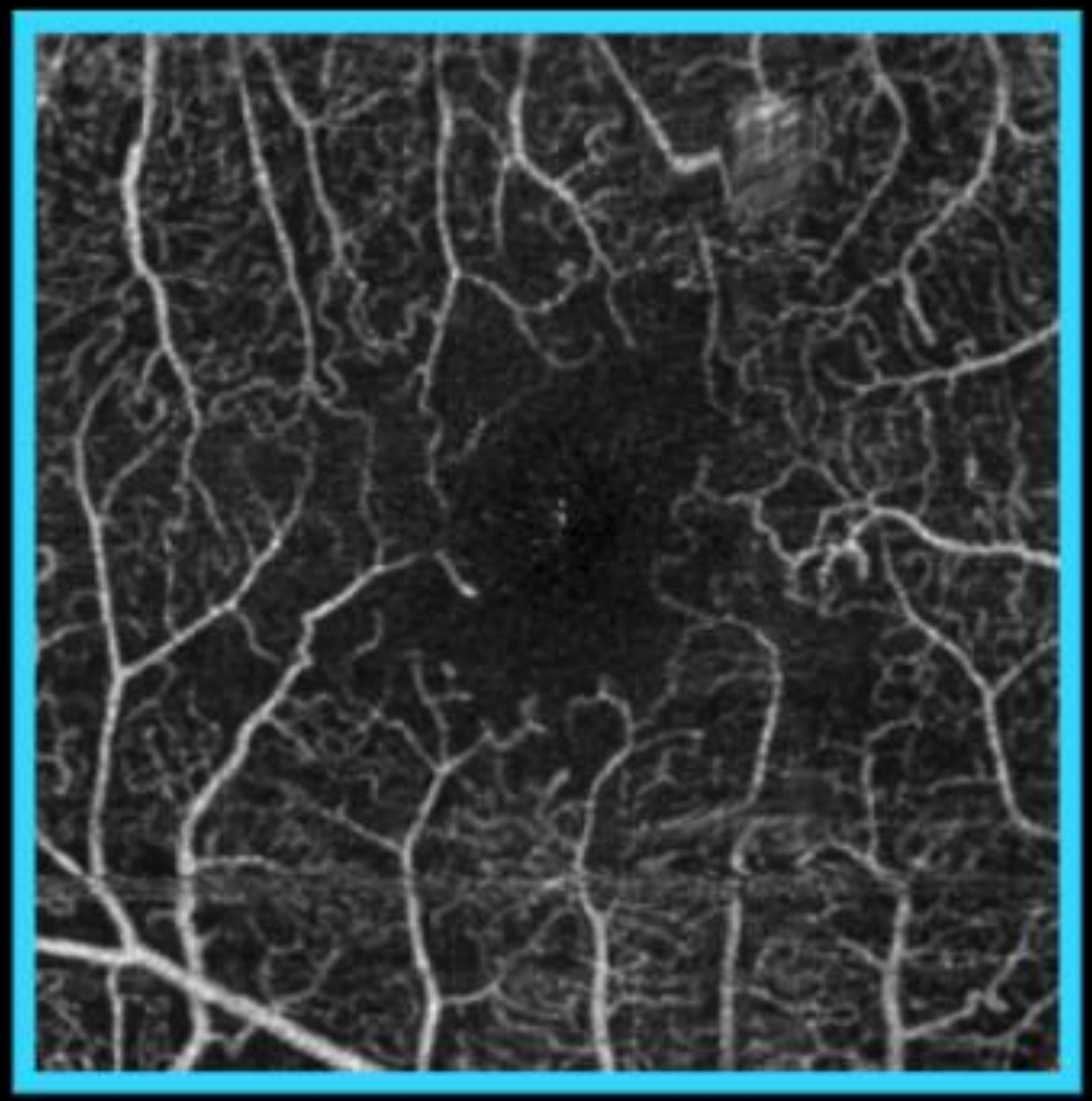
Decorrelation

Field of View (8 x 8 mm)

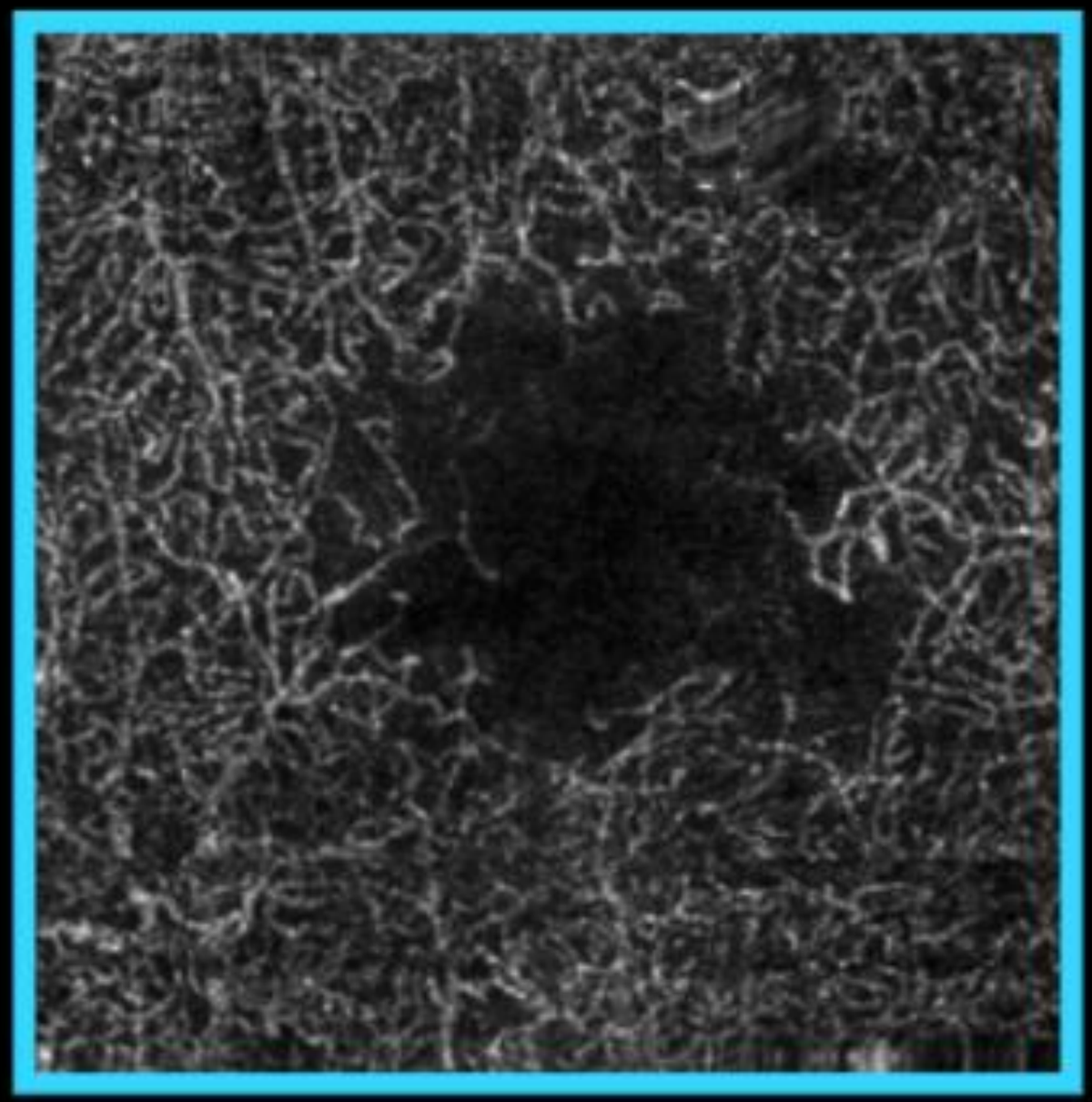
Projection

Field of View (2 x 2 mm)

OCTA: macular ischaemia

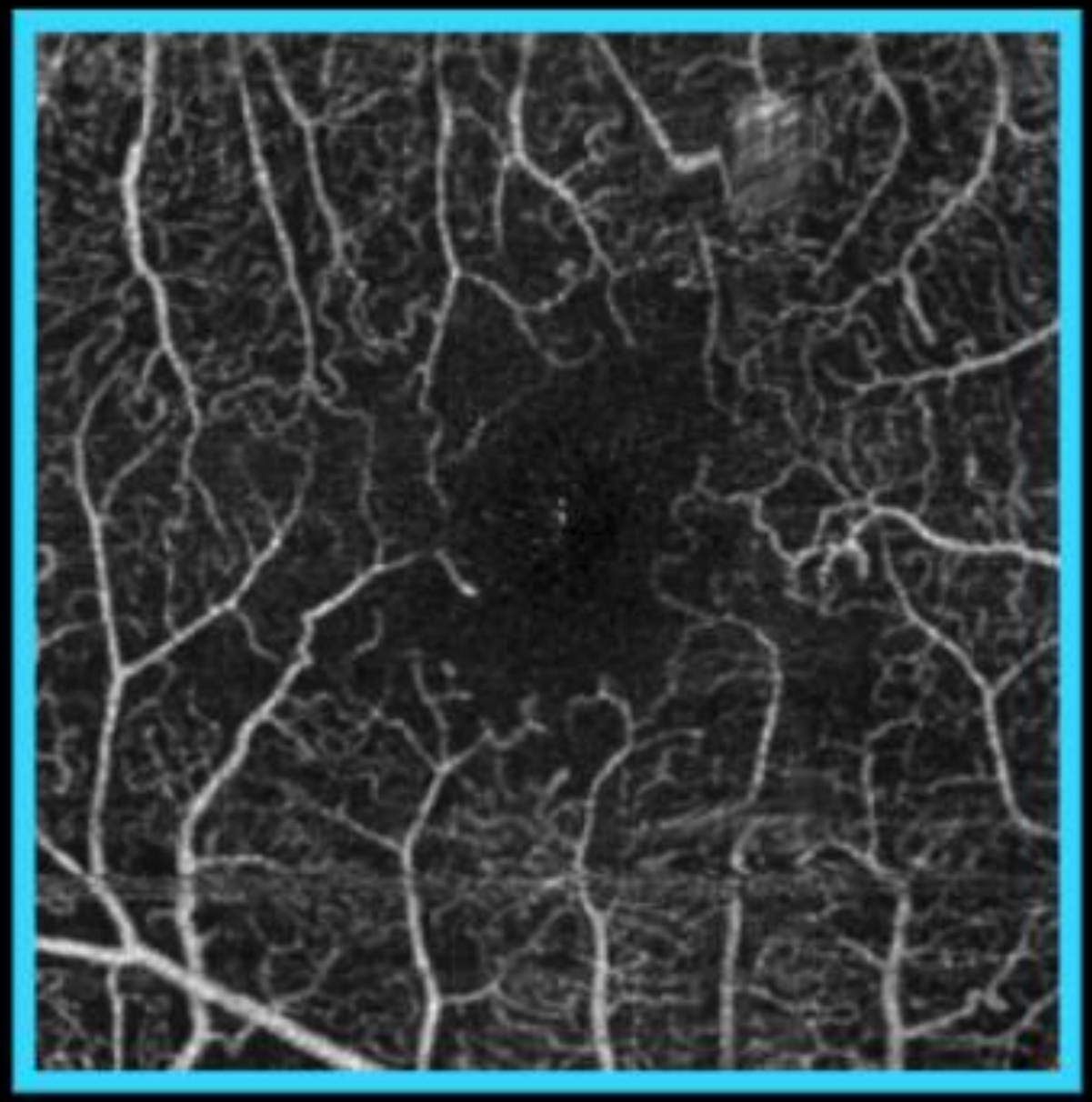


Superficial



Deep

OCTA: “crisper” detail

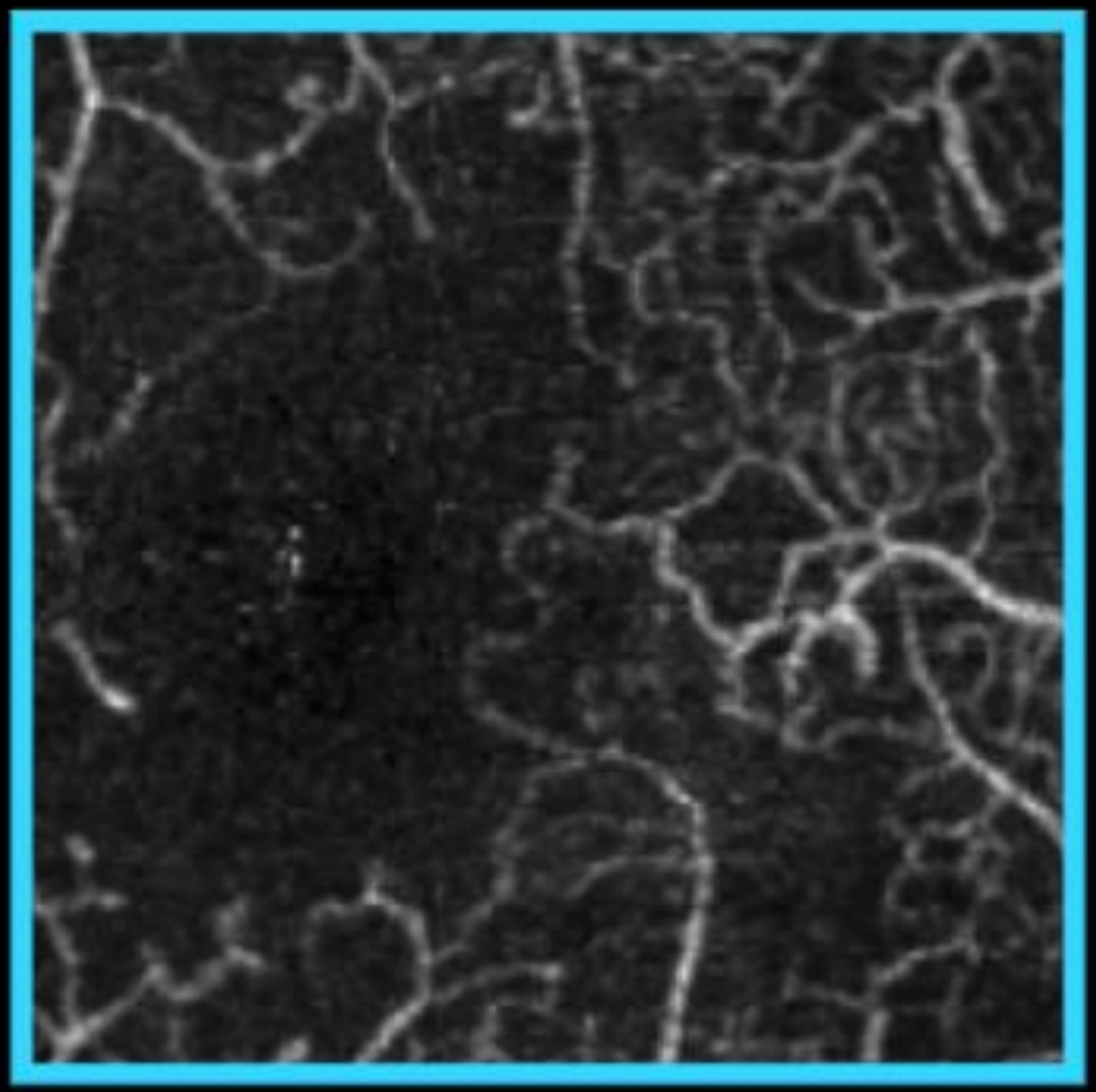


Superficial

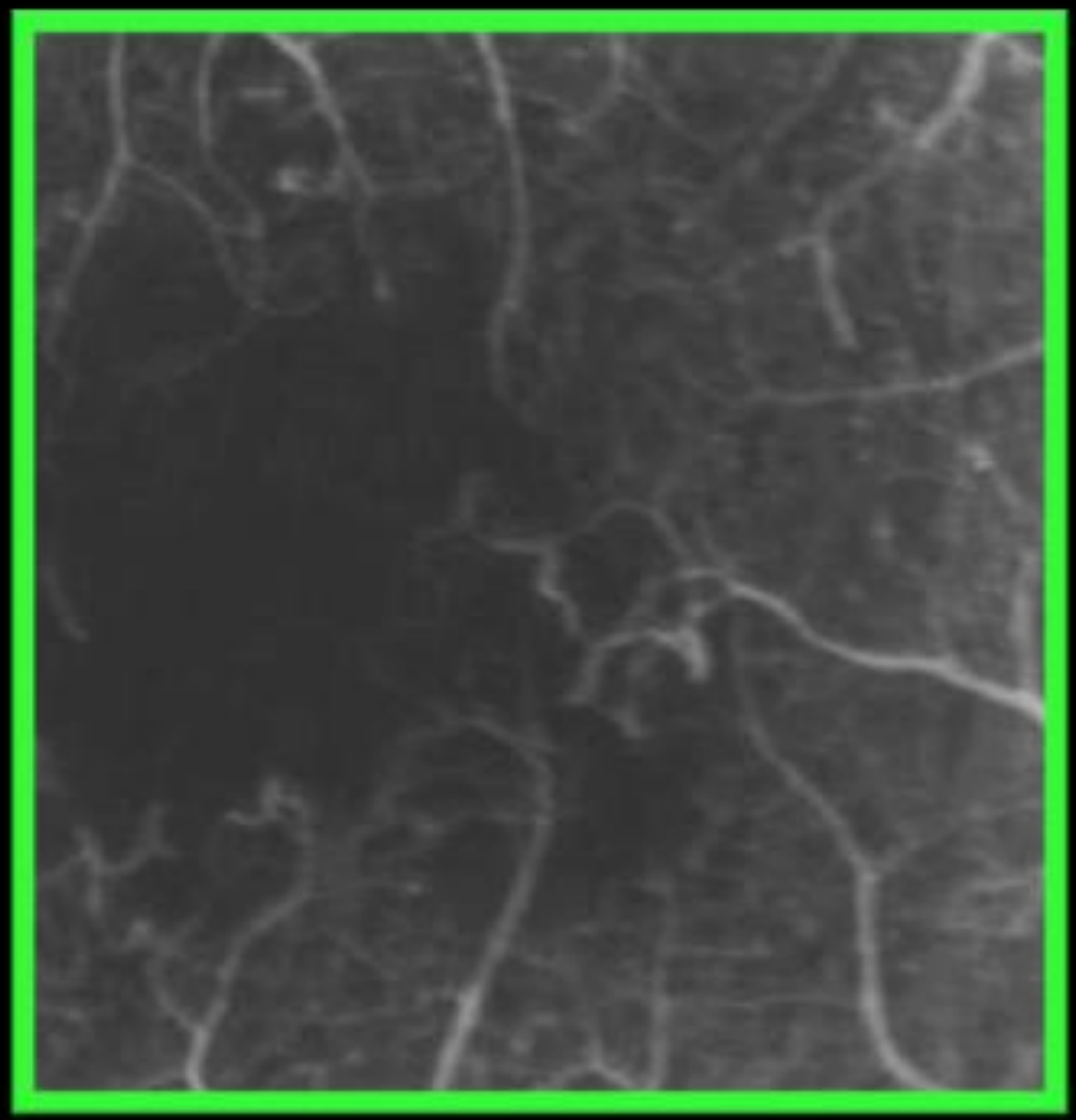
FA

Ischaemia

OCTA: zoom



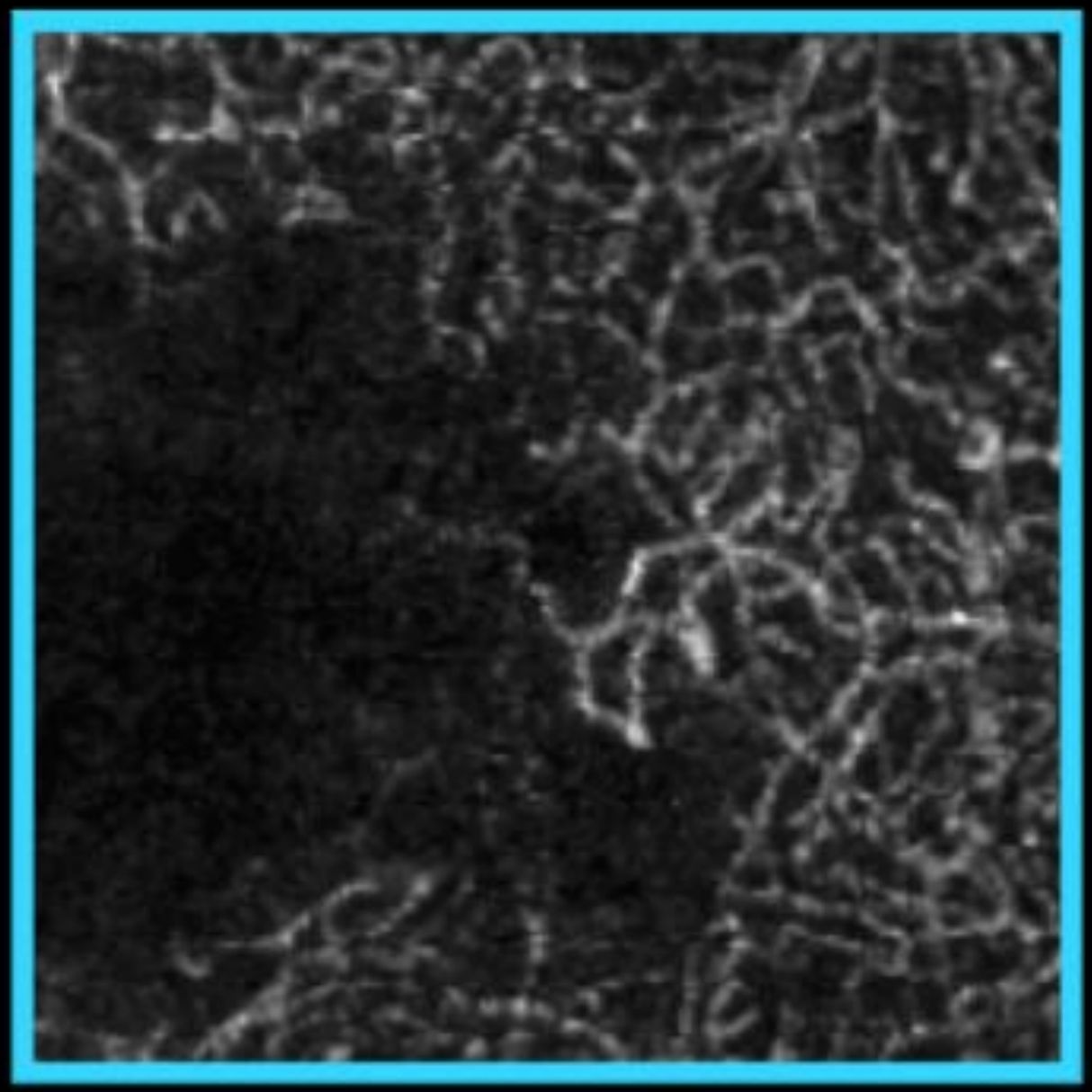
Superficial



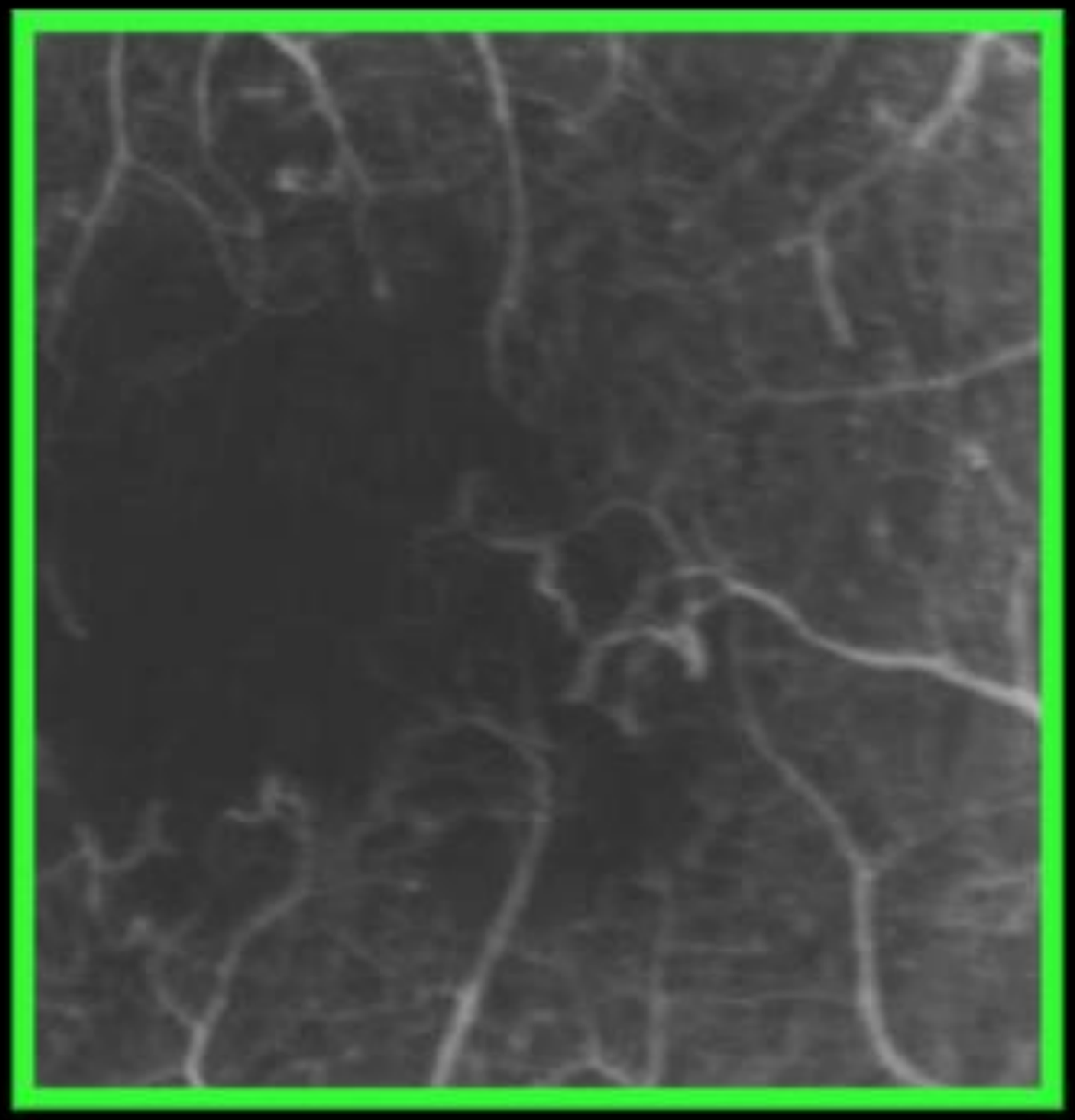
FA

Ischaemia

OCTA: additional depth information



Superficial



FA

Retina

The Evaluation of Diabetic Macular Ischemia Using Optical Coherence Tomography Angiography

Patrick D. Bradley,[1] Dawn A. Sim,[1] Pearse A. Keane,[1] João Carlos,[1,2] Rupesh Agrawal,[1] Adnan Tufail,[1] and Catherine A. Egan[1]

[1]Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom
[2]Hospital Garcia de Orta E.P.E., Almada, Portugal

Correspondence: Patrick D. Bradley, Moorfields Eye Hospital NHS Foundation Trust, 162 City Road, London EC1V 2PD, UK; patrickbradley01@gmail.com.

Submitted: August 24, 2015
Accepted: January 11, 2016

Citation: Bradley PD, Sim DA, Keane PA, et al. The evaluation of diabetic macular ischemia using optical coherence tomography angiography. *Invest Opbtbalmol Vis Sci*. 2016;57:626–631. DOI:10.1167/iovs.15-18034

Purpose. The purpose of this study was to compare optical coherence tomography (OCT) angiography to standard fluorescein angiography (FA) in the grading of diabetic macular ischemia.

Methods. In our study, OCT angiography and traditional FA images were acquired from 24 diabetic patients. The level of diabetic macular ischemia in the superficial capillary plexus was graded with standard Early Treatment Diabetic Retinopathy Study (ETDRS) protocols and a comparison between conventional FA and OCT angiography was performed. The deep vascular plexus and choriocapillaris were also graded for macular ischemia. Additionally, flow indices were analyzed for all OCT angiography images.

Results. We identified moderate agreement between diabetic macular ischemia grades for conventional FA and OCT angiography (weighted κ of 0.53 and 0.41). In addition, the intergrader agreement for the superficial, deep, and choriocapillaris scores was substantial (weighted κ of 0.65, 0.61, and 0.65, respectively). Finally, the parafoveal flow indices were shown to have a statistically significant relationship with diabetic macular ischemia grades for the superficial capillary plexus ($P = 0.04$) and choriocapillaris ($P = 0.036$), with a trend toward significance for the deep capillary plexus ($P = 0.13$).

Retina

The Evaluation of Diabetic Macular Ischemia Using Optical Coherence Tomography Angiography

Patrick D. Bradley,[1] Dawn A. Sim,[1] Pearse A. Keane,[1] João Cardoso,[1,2] Rupesh Agrawal,[1] Adnan Tufail,[1] and Catherine A. Egan[1]

[1]Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom
[2]Hospital Garcia de Orta E.P.E., Almada, Portugal

Correspondence: Patrick D. Bradley, Moorfields Eye Hospital NHS Foundation Trust, 162 City Road, London EC1V 2PD, UK; patrickbradley01@gmail.com

Submitted: August 24, 2015
Accepted: January 11, 2016

Citation: Bradley PD, Sim DA, Keane PA, et al. The evaluation of diabetic macular ischemia using optical coherence tomography angiography. *Invest Ophthalmol Vis Sci*. 2016;57:626–631. DOI:10.1167/iovs.15-18034

Purpose. To evaluate the agreement between optical coherence tomography (OCT) angiography to standard fluorescein angiography (FA) in the grading of diabetic macular ischemia.

Methods. Optical coherence tomography angiography images were acquired from 24 diabetic patients. The level of diabetic macular ischemia in the superficial capillary plexus was graded with standard Early Treatment Diabetic Retinopathy Study (ETDRS) protocols and a comparison between conventional FA and OCT angiography was performed. The deep vascular plexus and choriocapillaris were also graded for macular ischemia. Additionally, flow indices were analyzed for all OCT angiography images.

Results. We identified moderate agreement between diabetic macular ischemia grades for conventional FA and OCT angiography (weighted κ of 0.53 and 0.41). In addition, the intergrader agreement for the superficial, deep, and choriocapillaris scores was substantial (weighted κ of 0.65, 0.61, and 0.65, respectively). Finally, the parafoveal flow indices were shown to have a statistically significant relationship with diabetic macular ischemia grades for the superficial capillary plexus ($P = 0.04$) and choriocapillaris ($P = 0.036$), with a trend toward significance for the deep capillary plexus ($P = 0.13$).

"Moderate agreement of DMI severity between FA & OCTA using ETDRS protocols"

"Substantial intergrader agreement of DMI severity with OCTA"

Diabetic macular ischaemia

Prevalence and national history data **not available**

Receives **less attention** due to the **lack of treatment options**

Relative rarity of clinically identifiable macular ischaemia in large prospective clinical trials using **fluorescein angiography**

How does diabetic macular ischaemia affect visual acuity?

The Effects of Macular Ischemia on Visual Acuity in Diabetic Retinopathy

Dawn A. Sim,[1,2] *Pearse A. Keane,*[1,2] *Javier Zarranz-Ventura,*[1,2,4] *Simon Fung,*[1] *Michael B. Powner,*[2] *Elise Platteau,*[1,3] *Catey V. Bunce,*[1,2] *Marcus Fruttiger,*[2] *Praveen J. Patel,*[1,2] *Adnan Tufail,*[1,2] *and Catherine A. Egan*[1]

Purpose. To investigate the impact of diabetic macular ischemia (DMI) on visual acuity (VA), through the analysis of novel fluorescein angiography (FA) parameters.

Methods. Data were retrospectively collected over a 6-month period. DMI severity was graded using Early Treatment Diabetic Retinopathy Study (ETDRS) protocols. Custom software was used to quantify areas of the foveal avascular zone (FAZ), and of capillary nonperfusion over the papillomacular nerve fiber layer bundle, and temporal macula, and associations tested with VA.

Results. A total of 488 patients with type 2 diabetes mellitus and FAs of sufficient quality to allow detailed quantitative analyses were included. ETDRS-DMI severity was graded as: none, 39.7%; questionable, 18.4%; mild, 25.2%; moderate, 11.0%; and severe, 5.6%. Median FAZ areas were 0.19 mm^2 (interquartile range [IQR], 0.13–0.25); 0.25 mm^2 (IQR, 0.18–0.32); 0.27 mm^2 (IQR, 0.19–0.38); 0.32 mm^2 (IQR, 0.25–0.54); and 0.78 mm^2 (IQR, 0.60–1.32), respectively, and were significantly different between all grades ($P < 0.002$), apart from "questionable" versus "mild" grades. Significant associ-

describe the independent association of papillomacular nerve fiber bundle ischemia with reduced VA. (*Invest Ophthalmol Vis Sci.* 2013;54:2353–2360) DOI:10.1167/iovs.12-11103

Diabetic macular ischemia (DMI) is an important cause of visual impairment in patients with diabetic retinopathy[1,2]—in large part due to the devastating and irreversible visual loss that it causes in a minority of cases.[3] DMI is best-visualized using fluorescein angiography (FA), and is characterized by enlargement and disruption of the foveal avascular zone (FAZ), and by retinal capillary loss in other, noncontiguous areas of the macula ("capillary drop-out").[4–6] Standards for assessment of DMI severity were first established in the Early Treatment Diabetic Retinopathy Study (ETDRS) in the 1980s.[5] Since then, numerous studies have demonstrated a link between the presence of DMI and the loss of visual function.[3,7–10] Furthermore, other studies suggest that, in patients receiving treatment for diabetic macular edema (DME), the coexistence of DMI may have an adverse effect on outcomes, or limit the benefits of treatments, regardless of

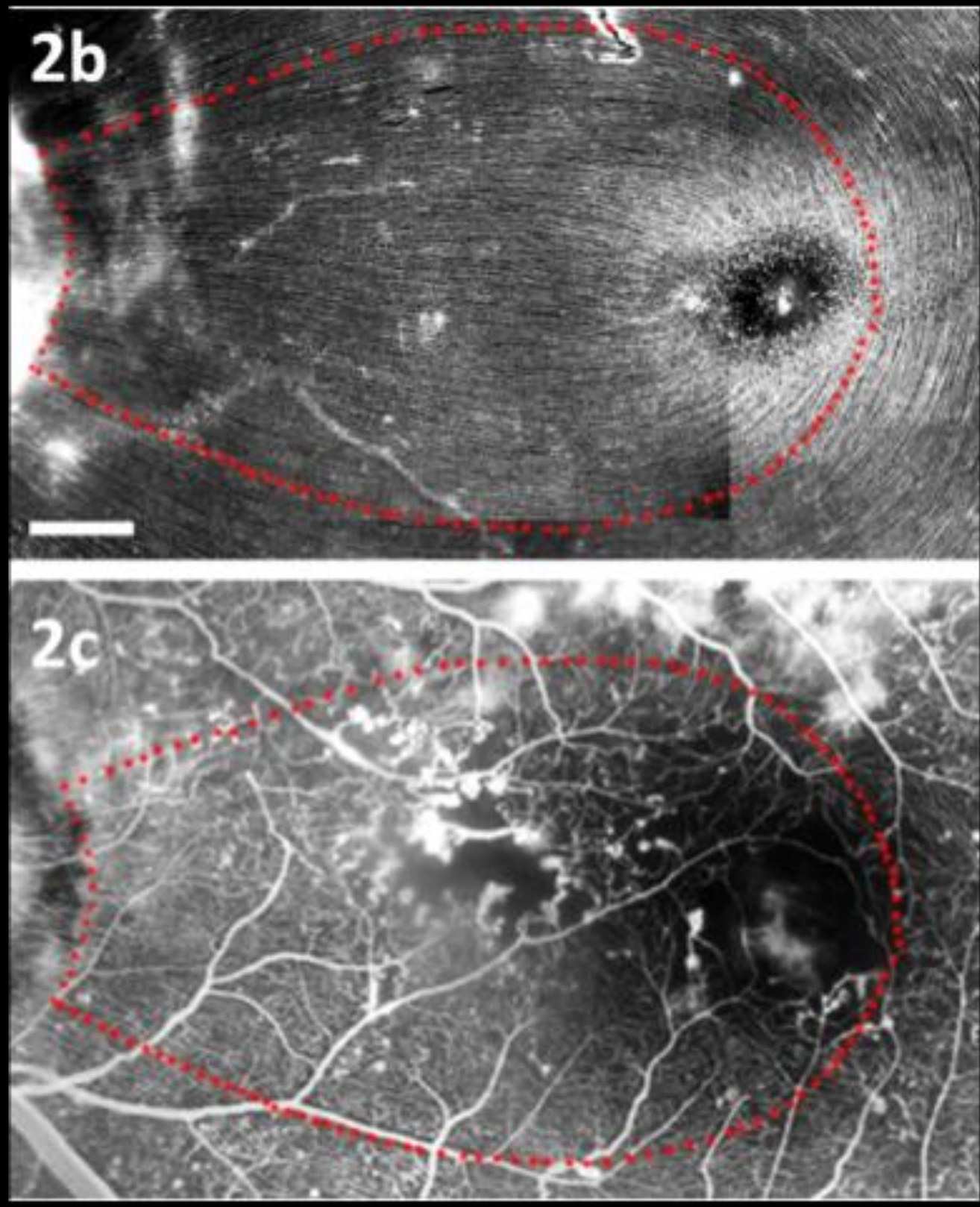
“Visual Acuity is preserved in milder grades of DMI and impaired in moderate and severe DMI”

Location, location, location

Papillomacular Nerve fibre bundle

Capillary non perfusion

Affects Visual Acutiy



How quickly does diabetic macular ischaemia progress?

Predictive Factors for the Progression of Diabetic Macular Ischemia

DAWN A. SIM, PEARSE A. KEANE, JAVIER ZARRANZ-VENTURA, CATEY V. BUNCE, MARCUS FRUTTIGER, PRAVEEN J. PATEL, ADNAN TUFAIL, AND CATHERINE A. EGAN

• PURPOSE: To investigate the predictive factors for diabetic macular ischemia progression through the analysis of fluorescein angiography (FA) parameters.

• DESIGN: Retrospective, longitudinal observational case series.

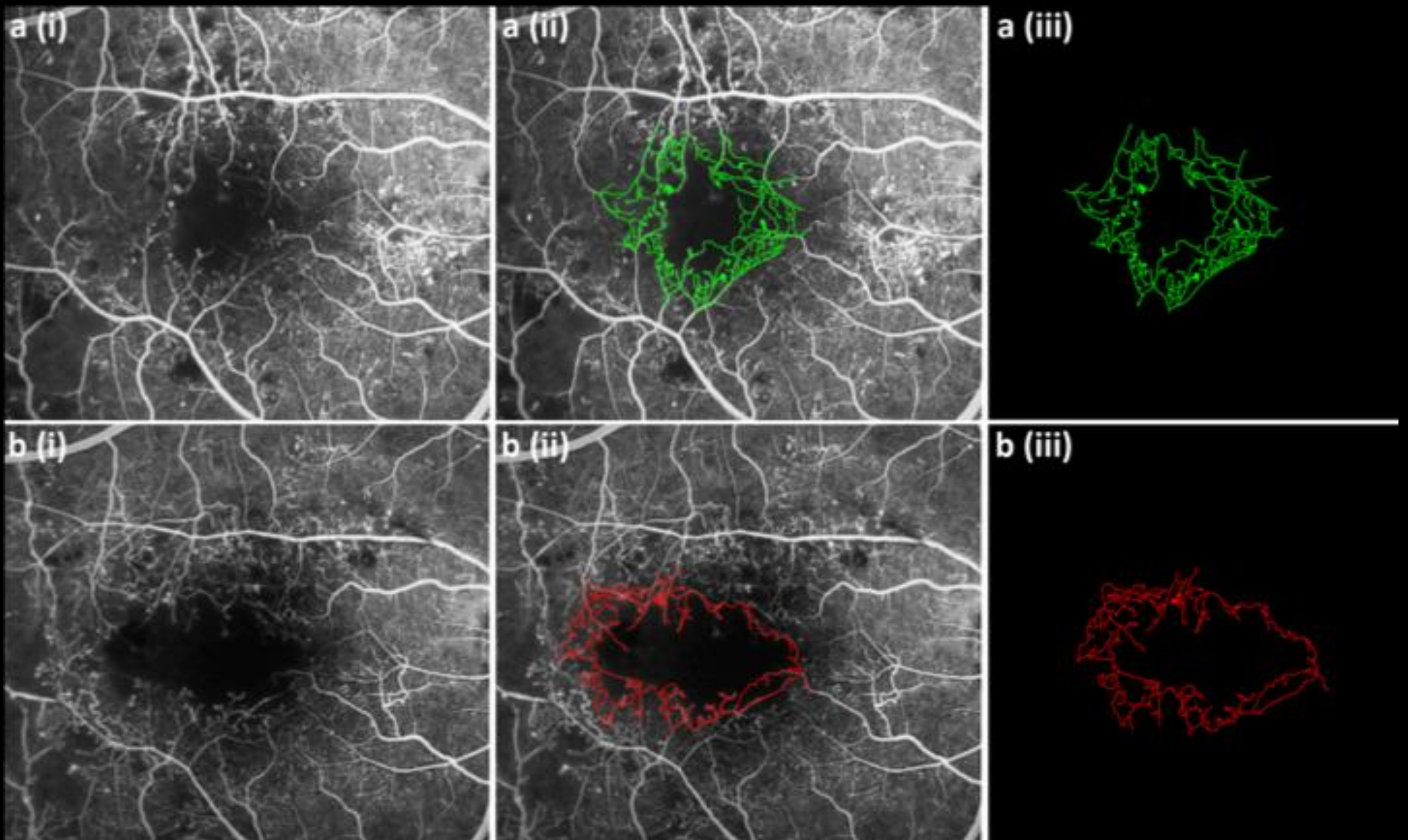
• METHODS: Data were collected from 79 eyes of 79 patients with type 2 diabetes mellitus. Macular ischemia severity was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) protocols and custom software used to quantify the foveal avascular zone (FAZ) area. Patients with ischemia grades "mild," "moderate," or "severe" and at least 2 macula-centered FA images over a minimum of 6 months were included. Main outcome measures were change in macular ischemia grades and FAZ enlargement rate (mm^2/year).

• RESULTS: The median FAZ areas in mild, moderate, and severe ischemia grades at baseline were 0.28, 0.37, and 0.73 mm^2, and significantly increased at the final FA (0.31, 0.41, and 1.23 mm^2) ($P = .001$). The median duration of follow-up was 27.5, 31.0, and 24.0 months, and was not significantly different between groups. FAZ

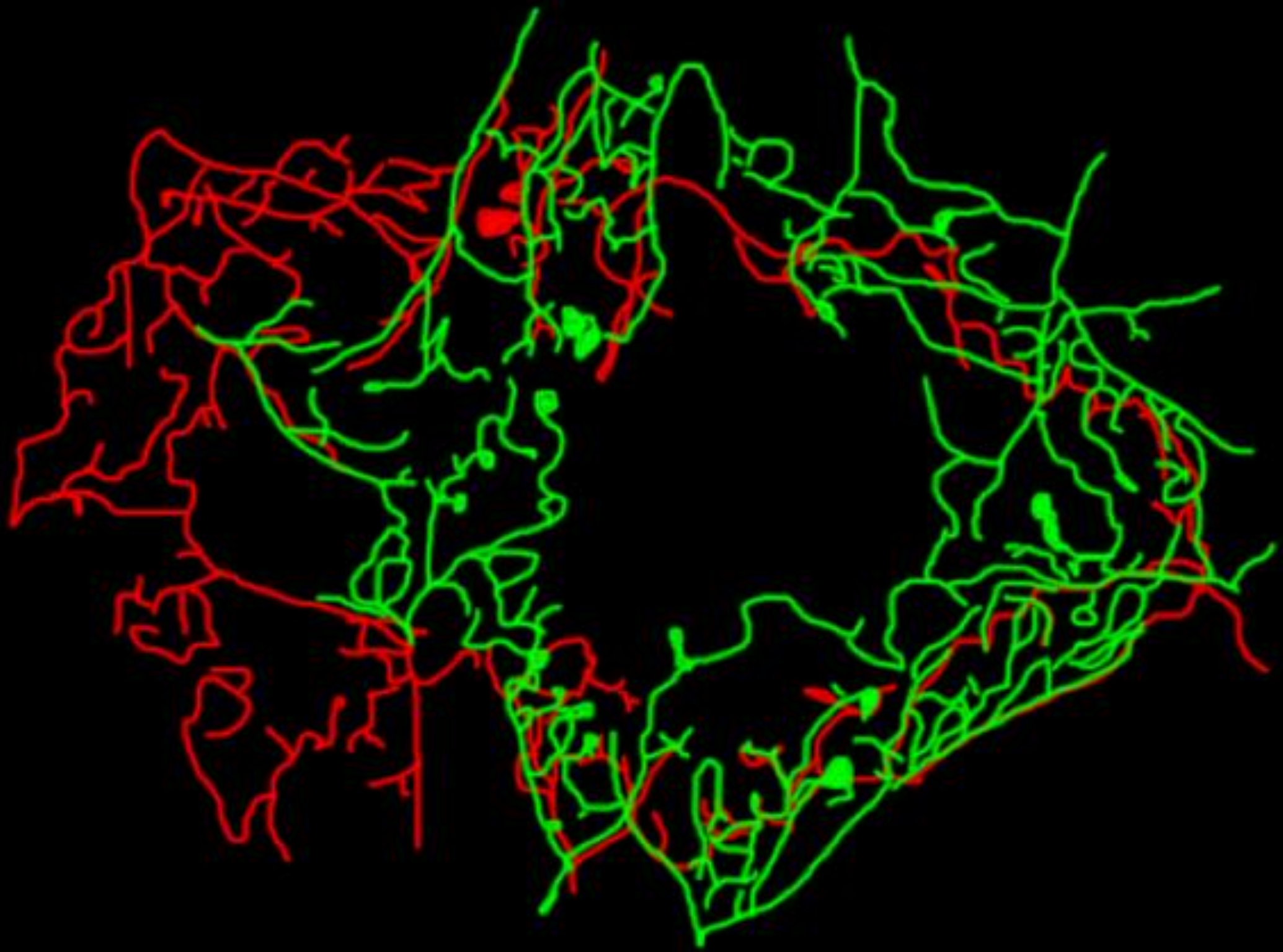
DIABETIC MACULAR ISCHEMIA WAS FIRST ESTABlished using fluorescein angiography (FA) in the Early Treatment Diabetic Retinopathy Study (ETDRS).[1–3] Owing to the limitations of angiography for its evaluation, diabetic macular ischemia has not been studied in the pivotal epidemiologic studies of diabetic retinopathy, and is not yet well understood.[4–6] Increasing our understanding of how quickly diabetic macular ischemia progresses, in whom it occurs, and its association with visual impairment is important in the clinical management of diabetic maculopathy. This may be of particular relevance because of emerging evidence for intravitreal pharmacotherapies, such as anti–vascular endothelial growth factor (VEGF), for the treatment of diabetic macular edema.[7–9]

The ongoing controversy regarding the potential adverse effects of anti-VEGF therapies on macular ischemia is largely based on case reports and noncomparative cases series—in patients receiving treatment for diabetic macular edema,[10–13] as an adjunctive treatment with pars

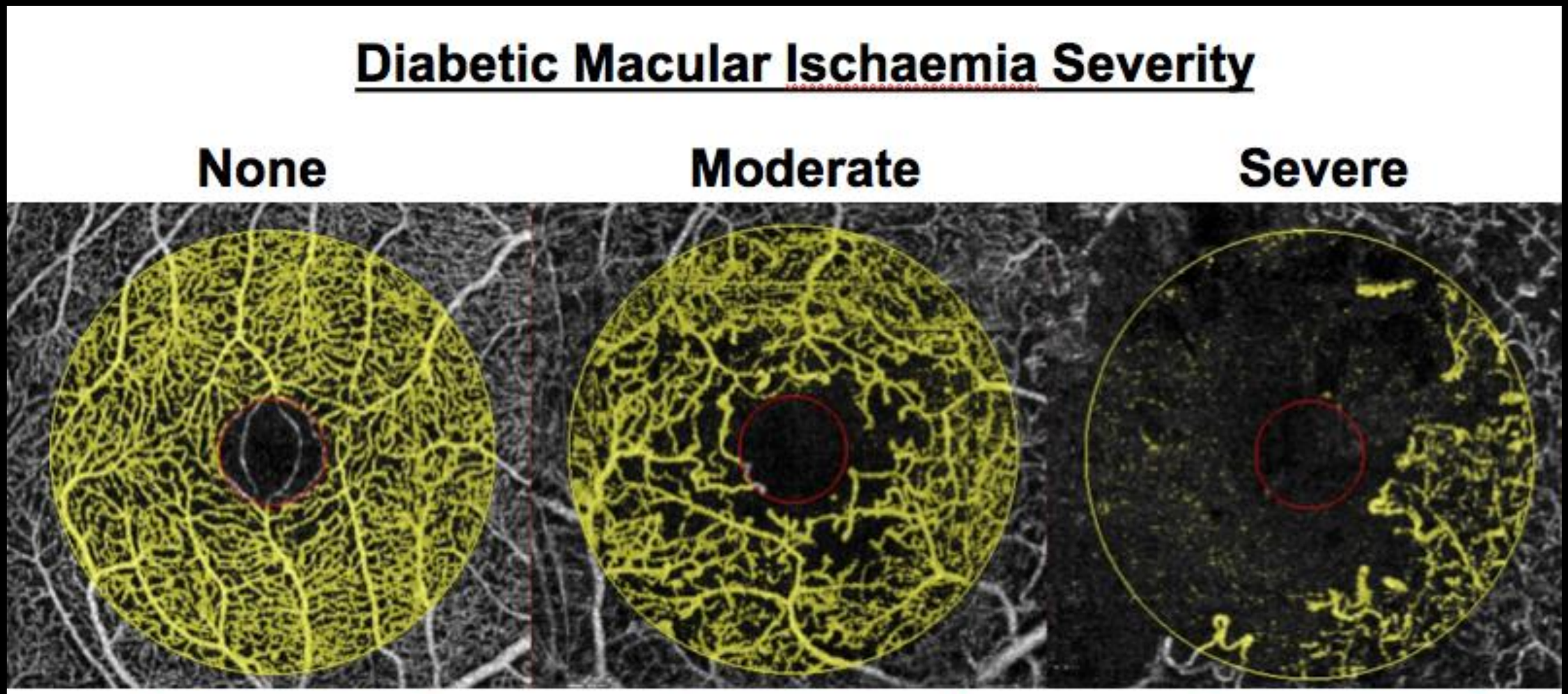
Progression over 2 years



FAZ remodelling



Quantification

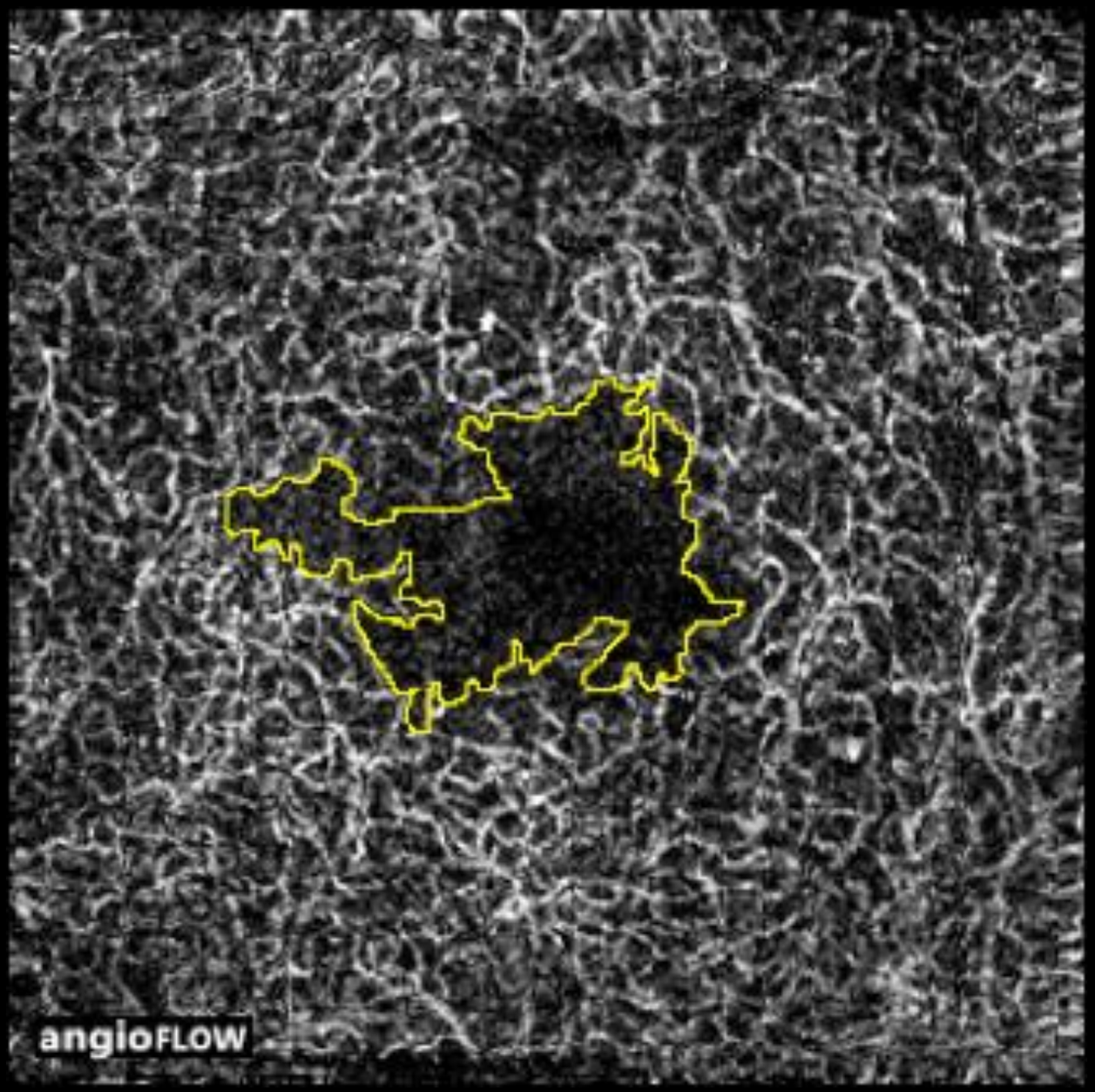


Superficial vascular plexus

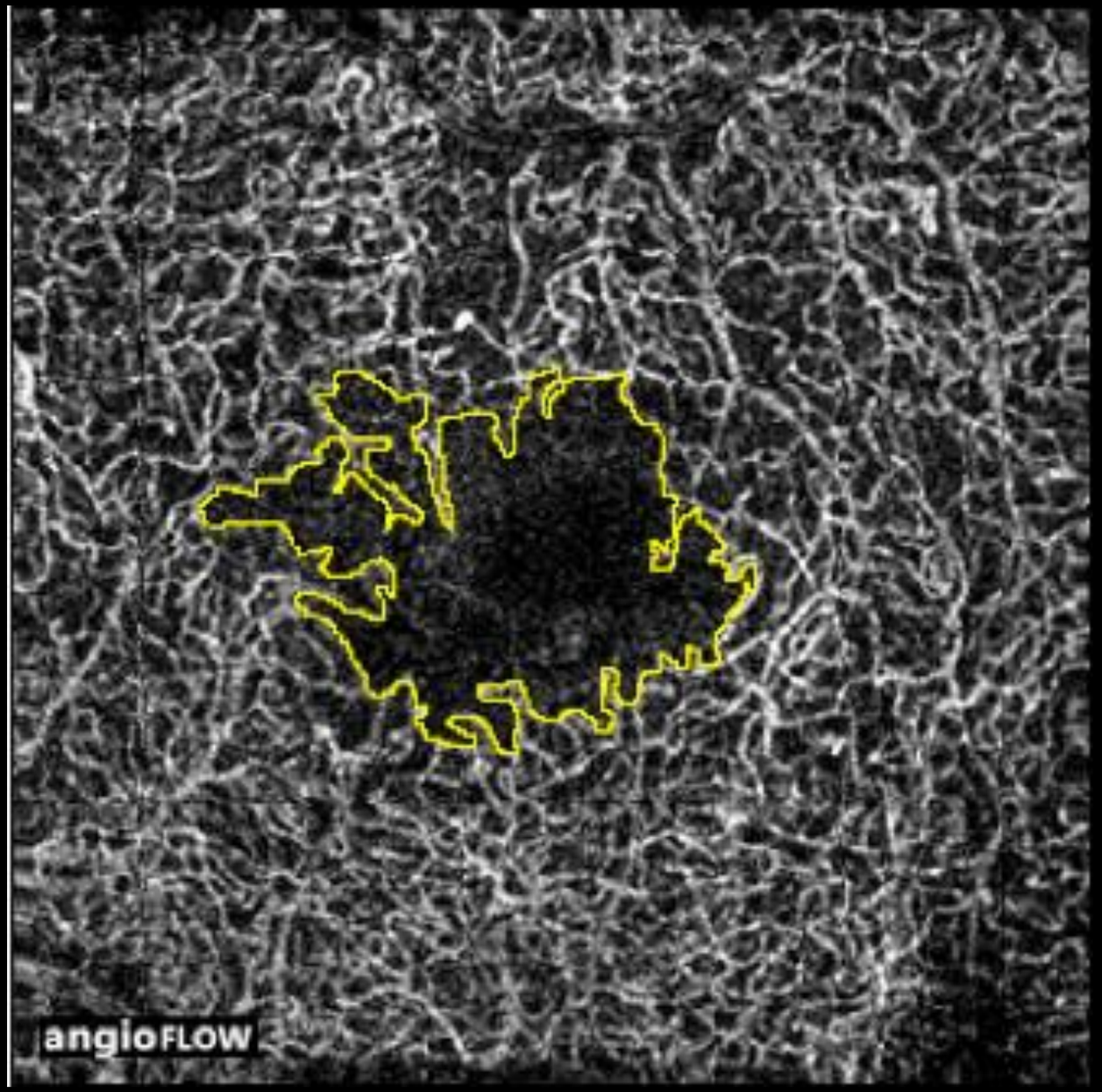
Baseline

12 months

Deep vascular plexus



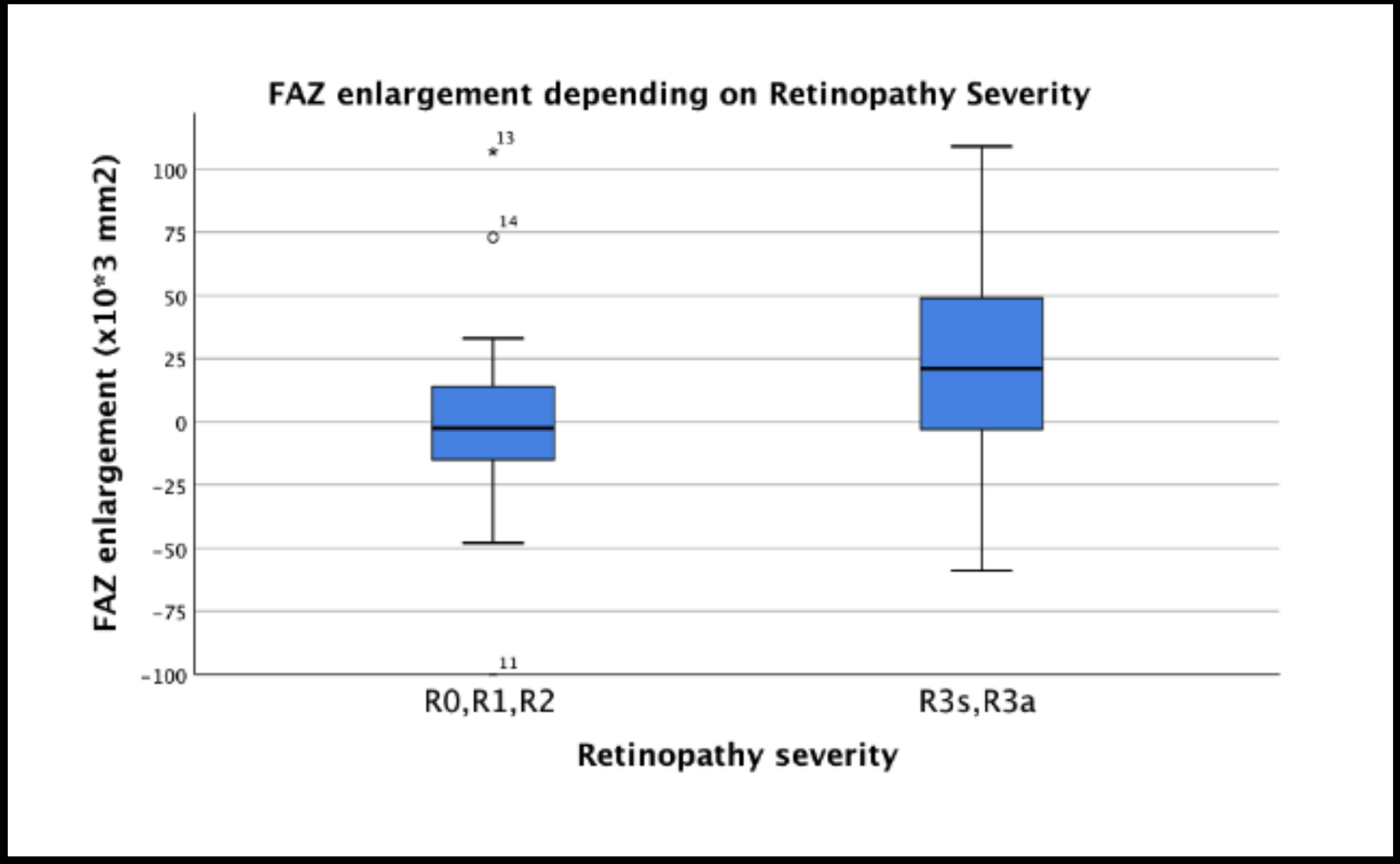
Baseline



12 months

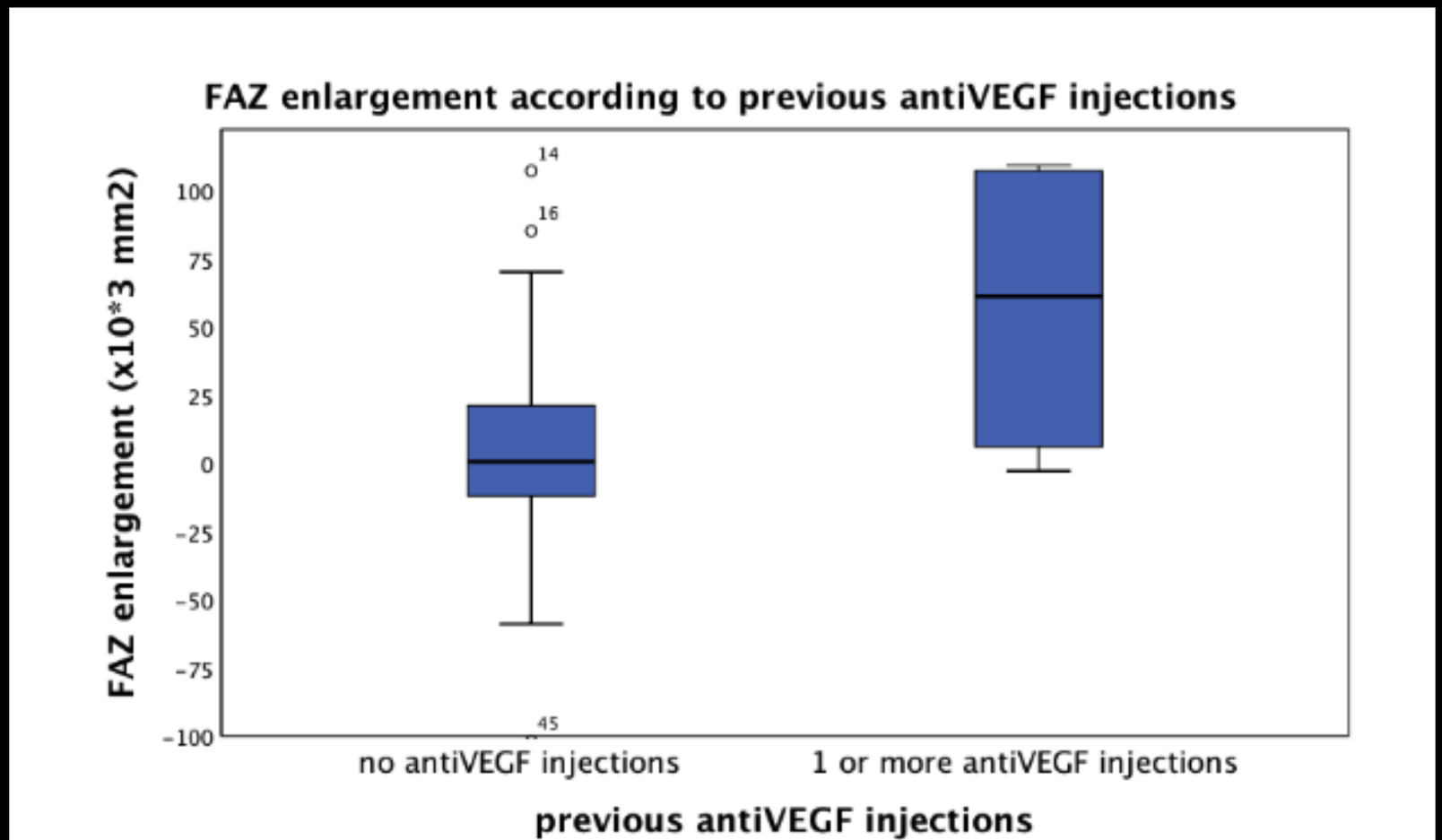
2 years+ experience…

- 2262 scans performed
- 248 patients with follow up scans



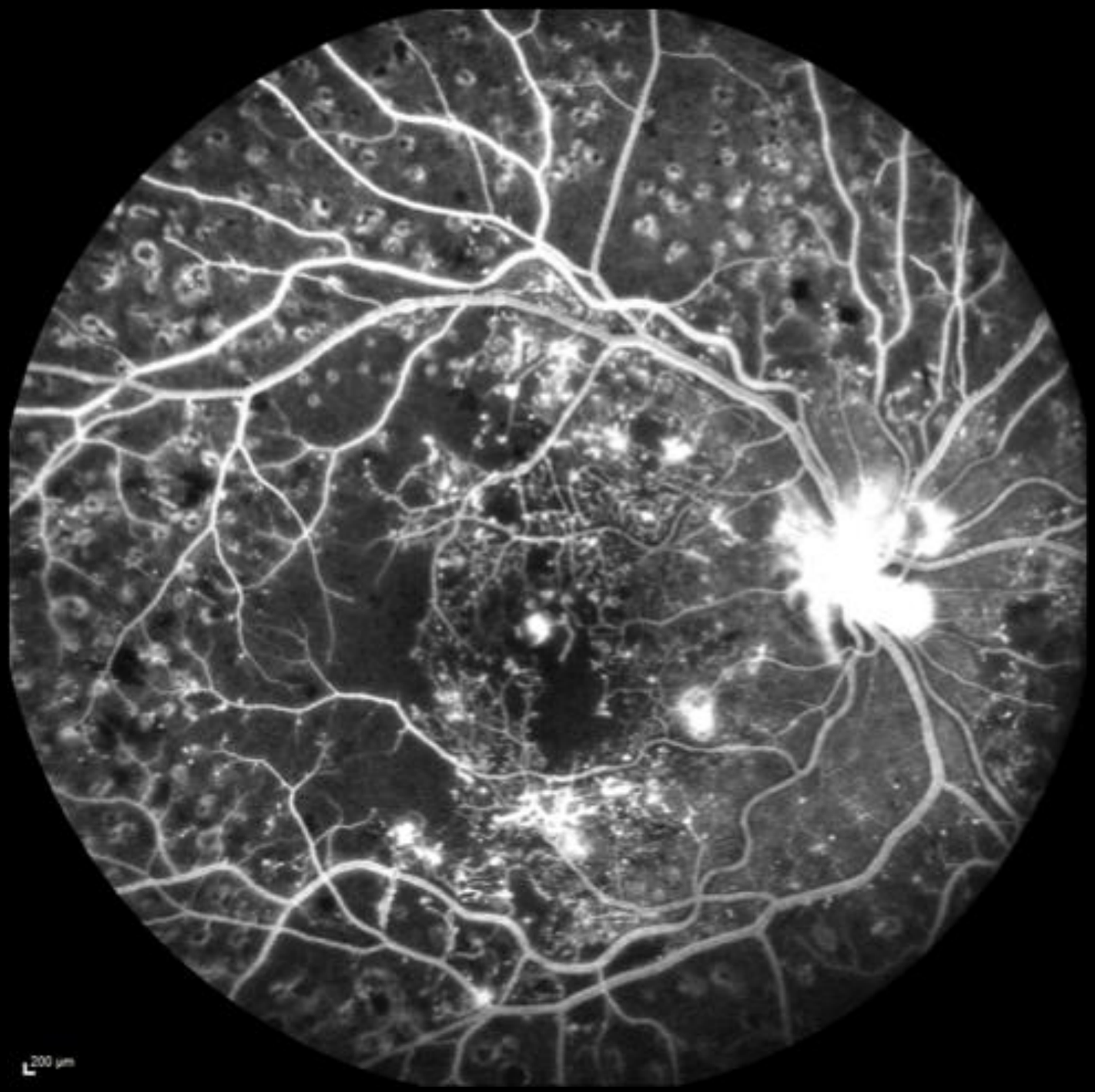
2 years+ experience…

- 2262 scans performed
- 248 patients with follow up scans



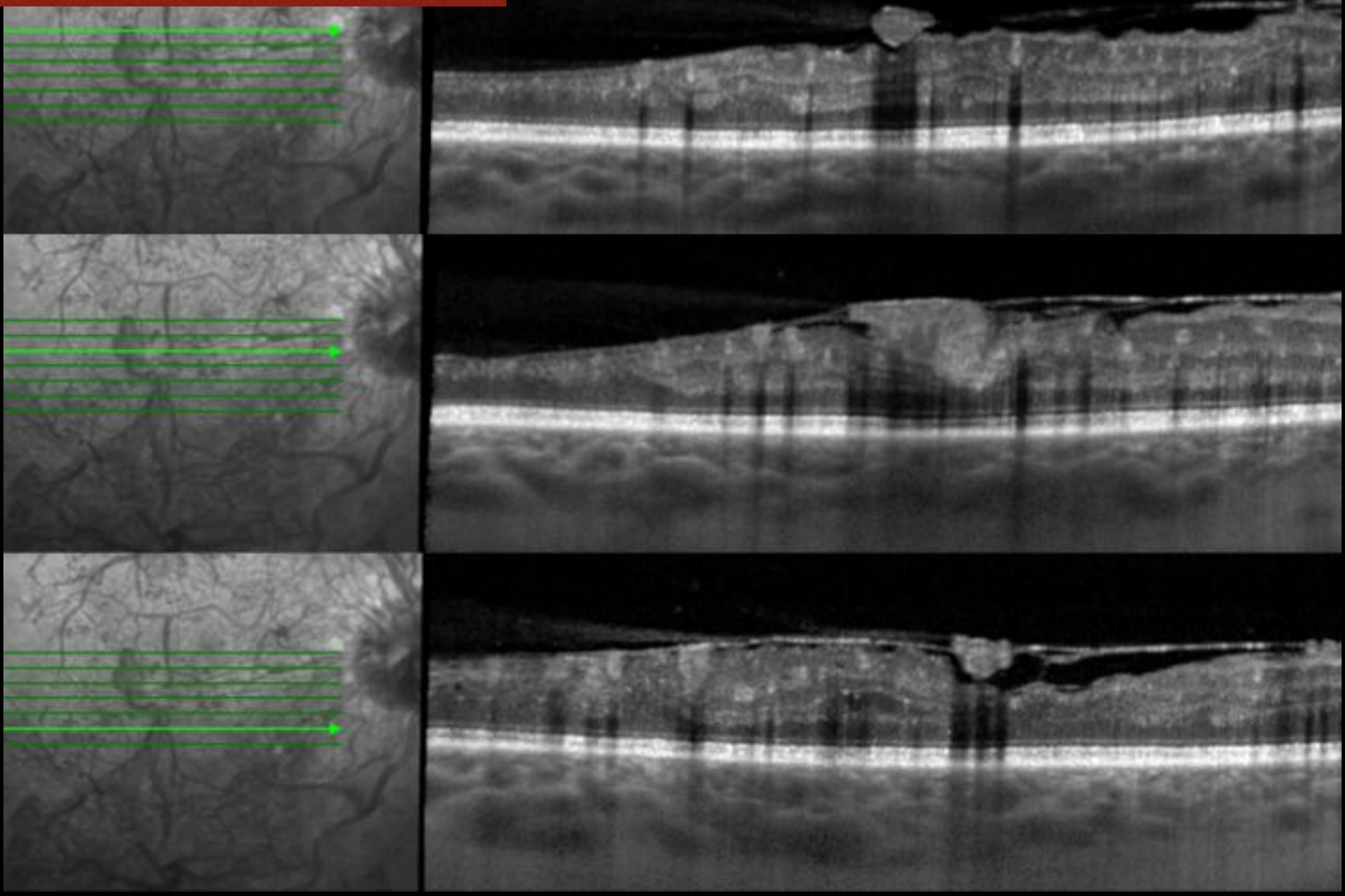
Neovascularisation

What about new vessels?

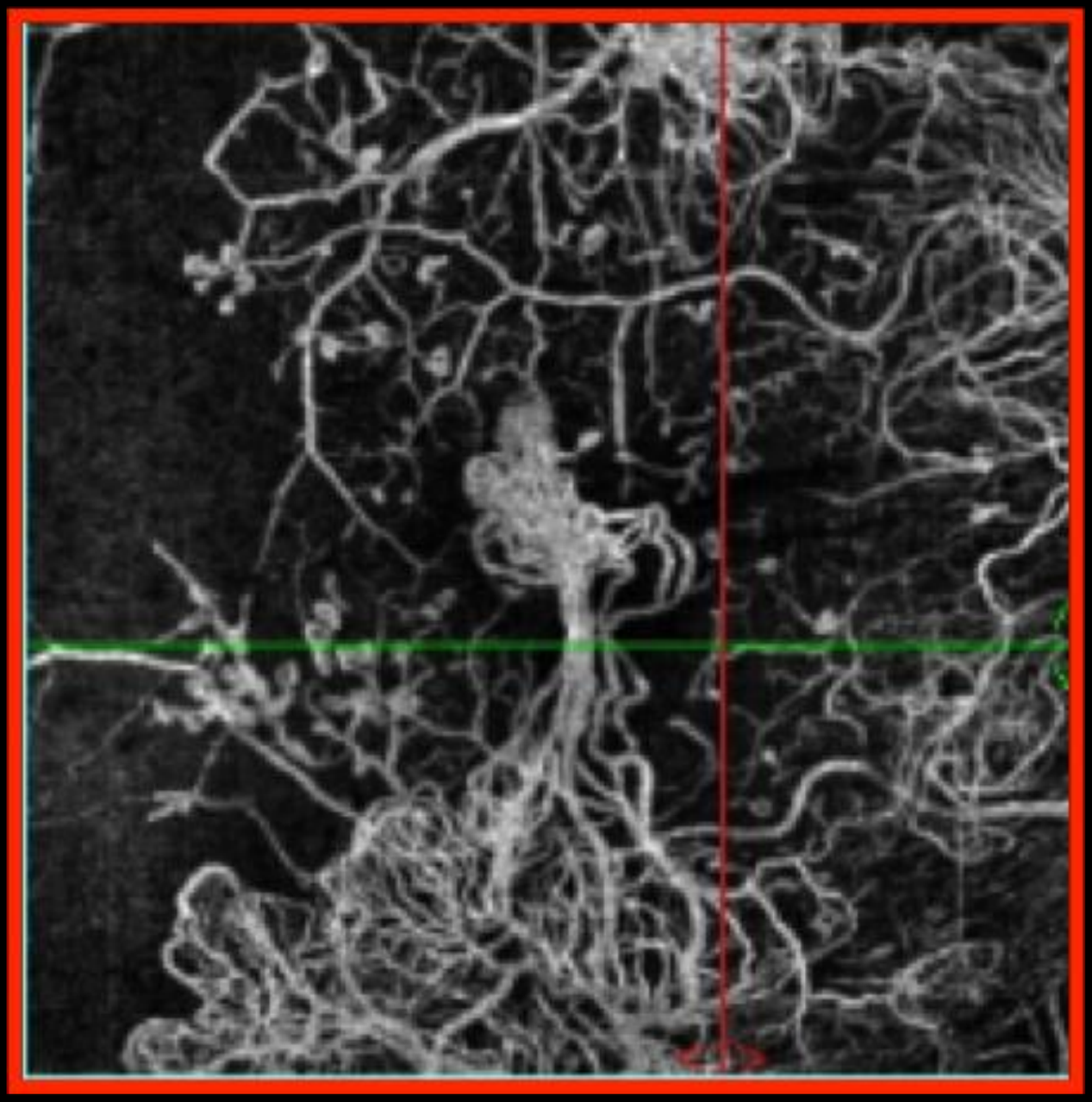


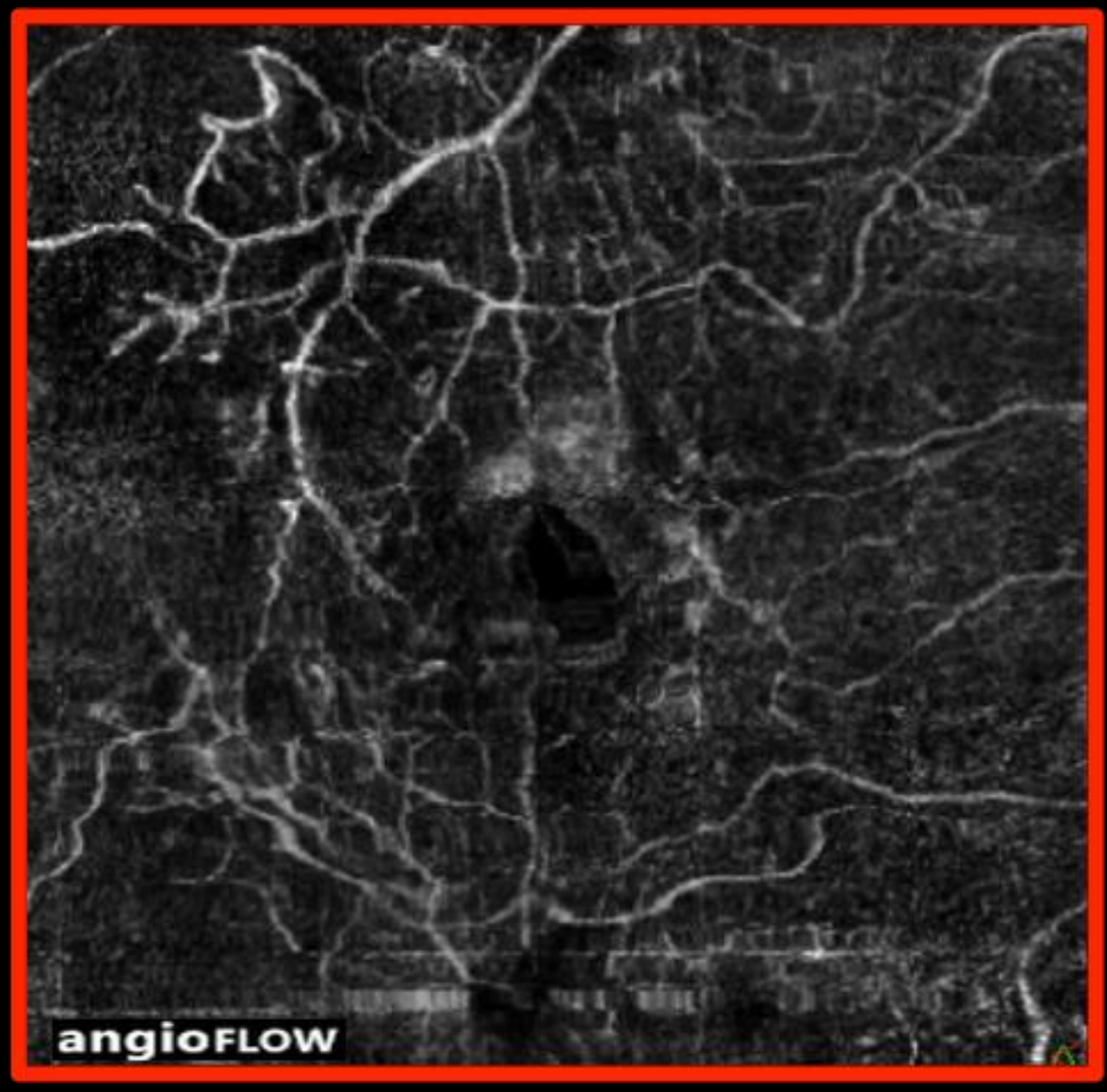
29 year old man
Poorly controlled
Type 1 DM

Neovascularisation



Neovascularisation



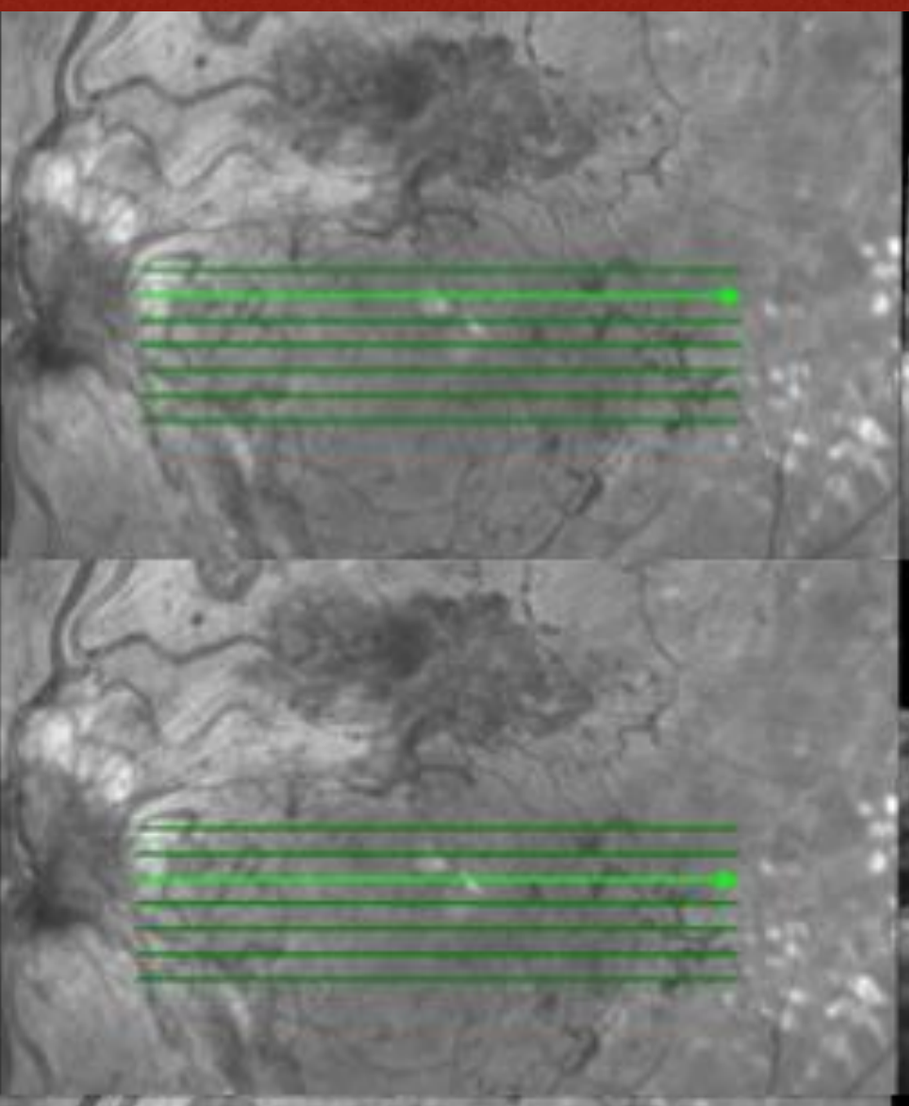


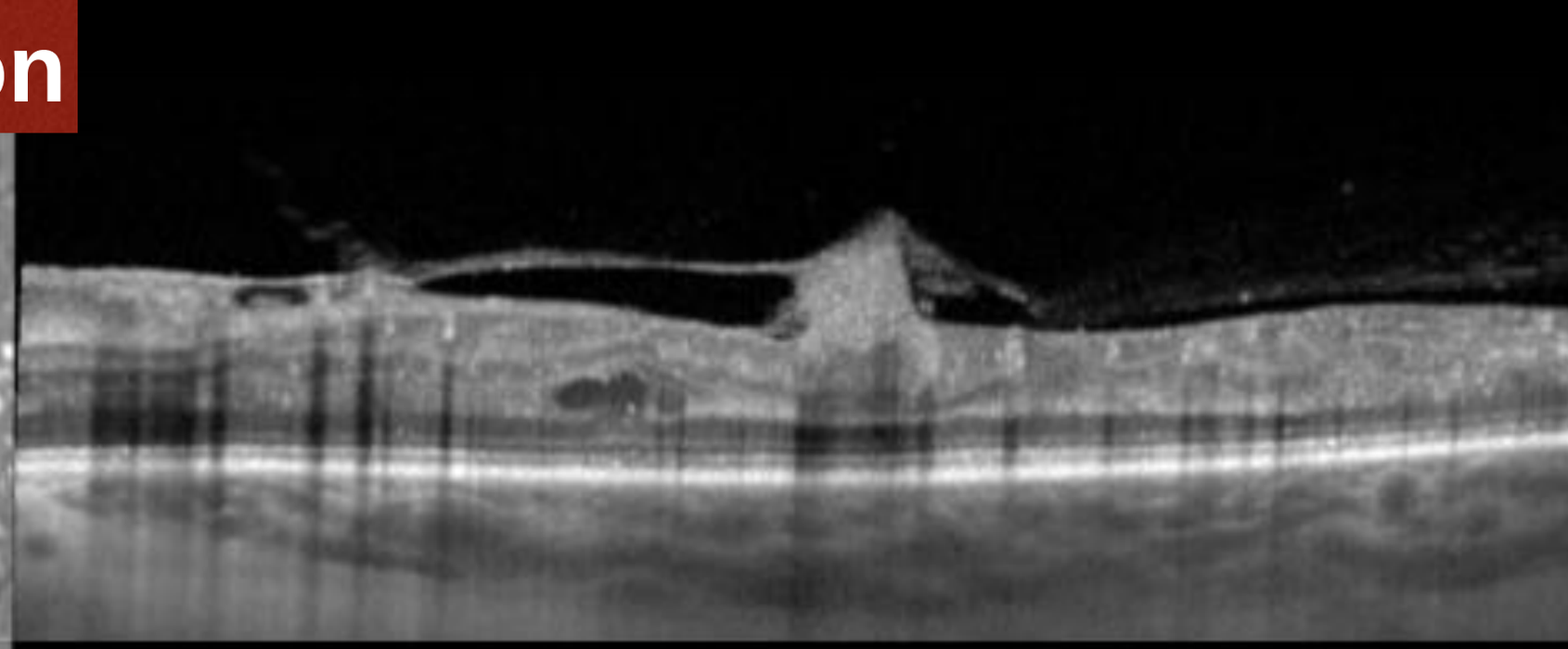
Before After treatment

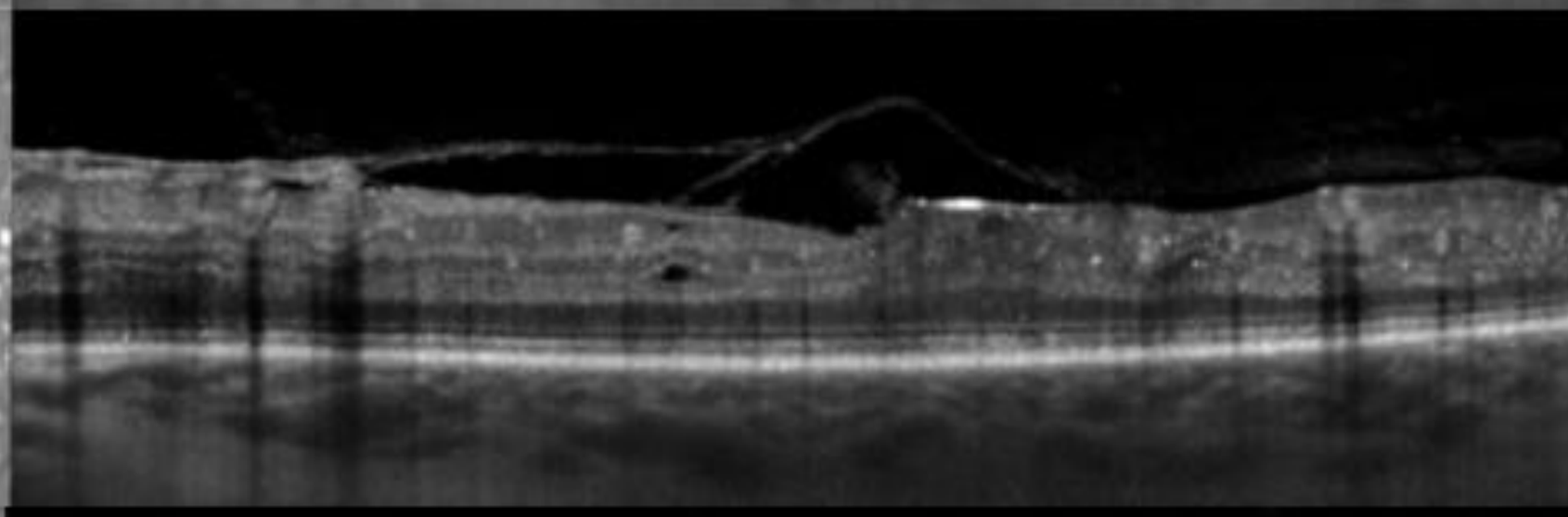
Macular NV

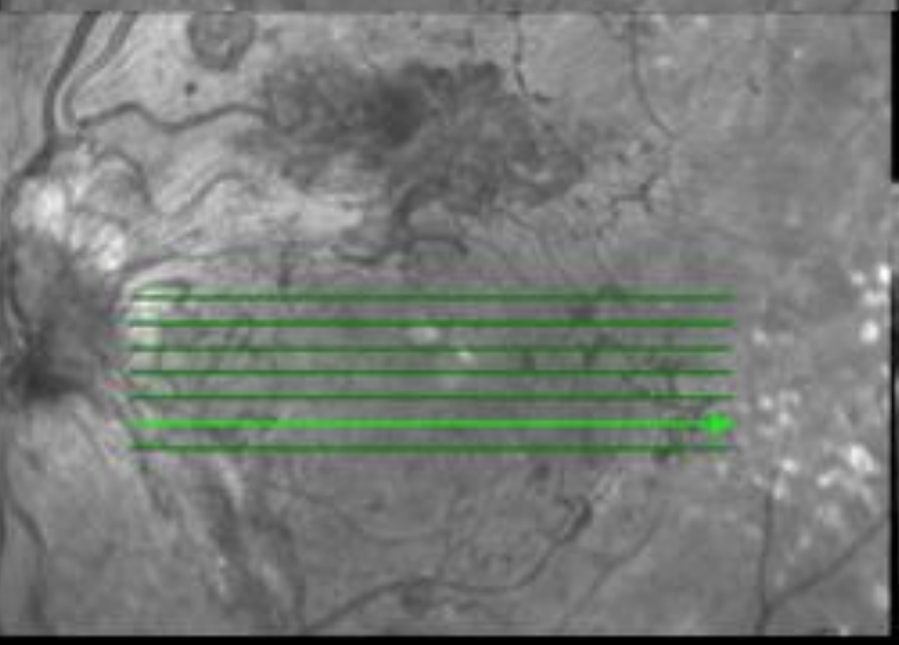
Neovascularisation

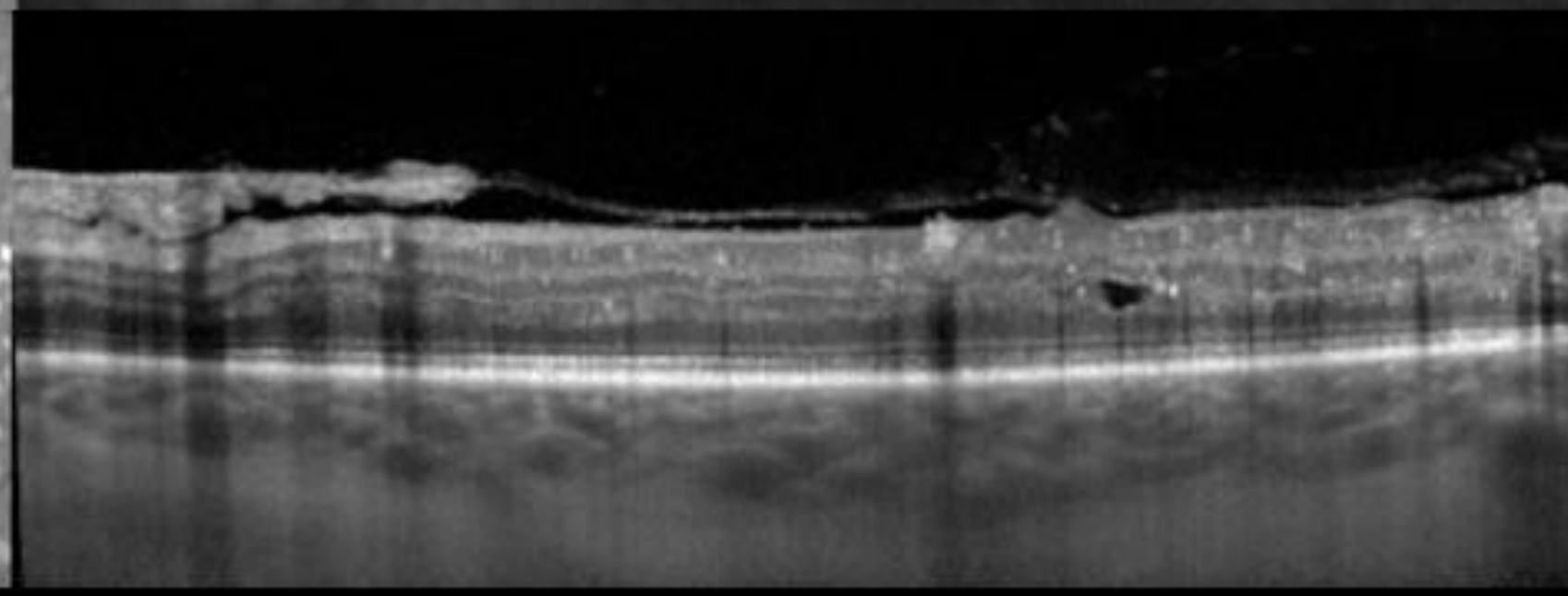
Neovascularisation



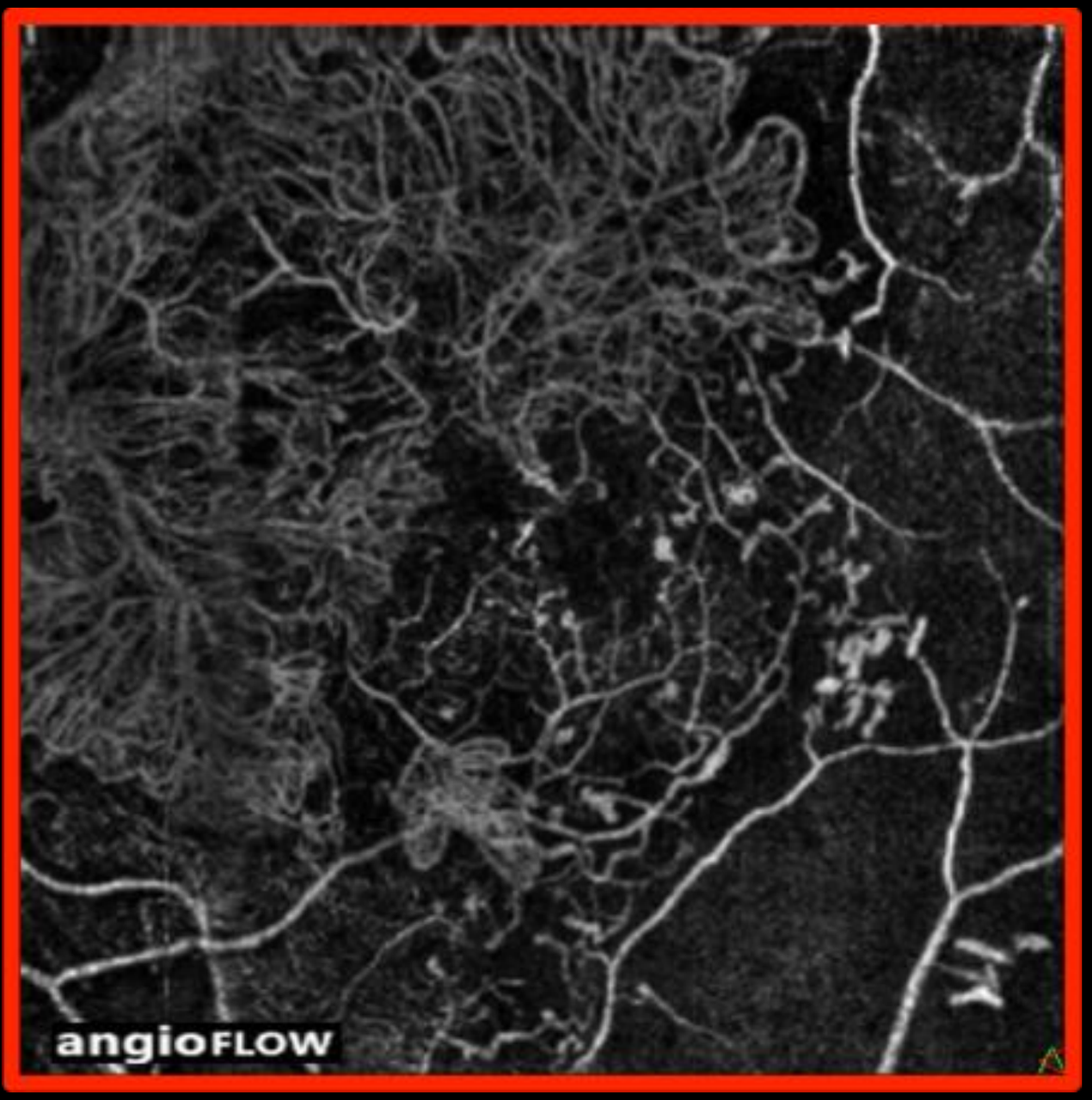




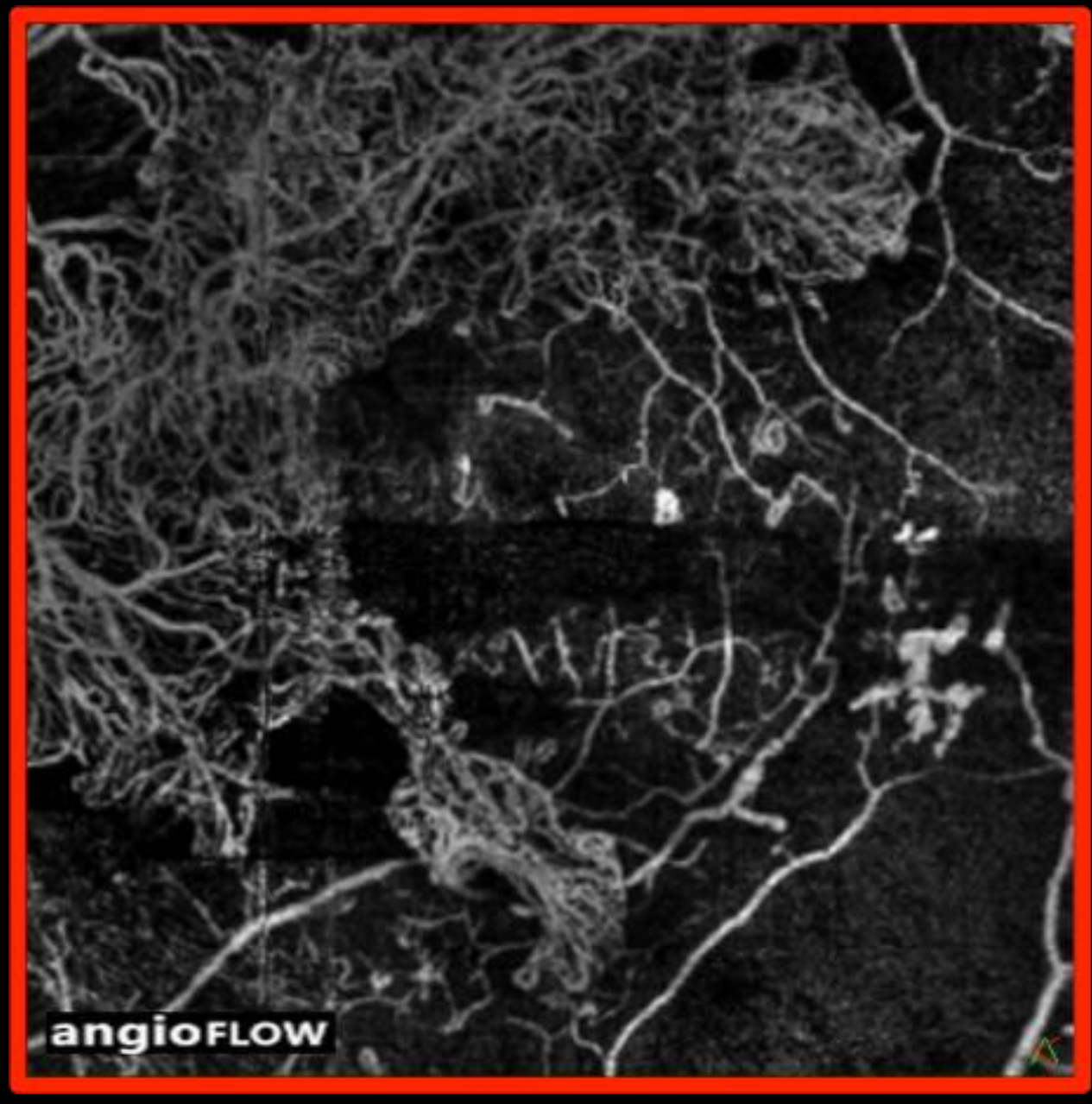




Neovascularisation



Before



After treatment

Early experience of OCTA

Use in conjunction with established retinal imaging techniques for:

Oedema

Ischaemia

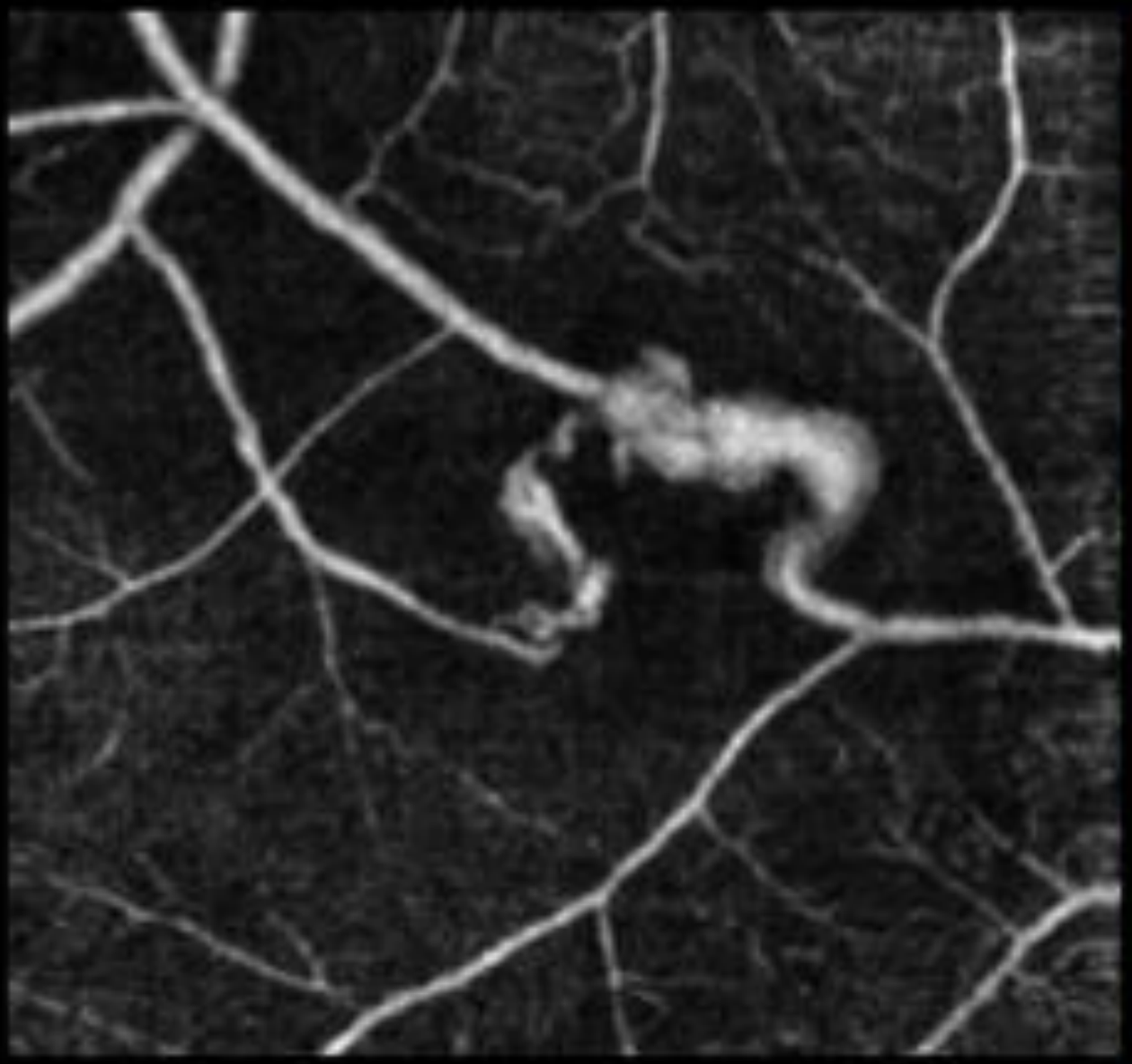
Neovascularisation

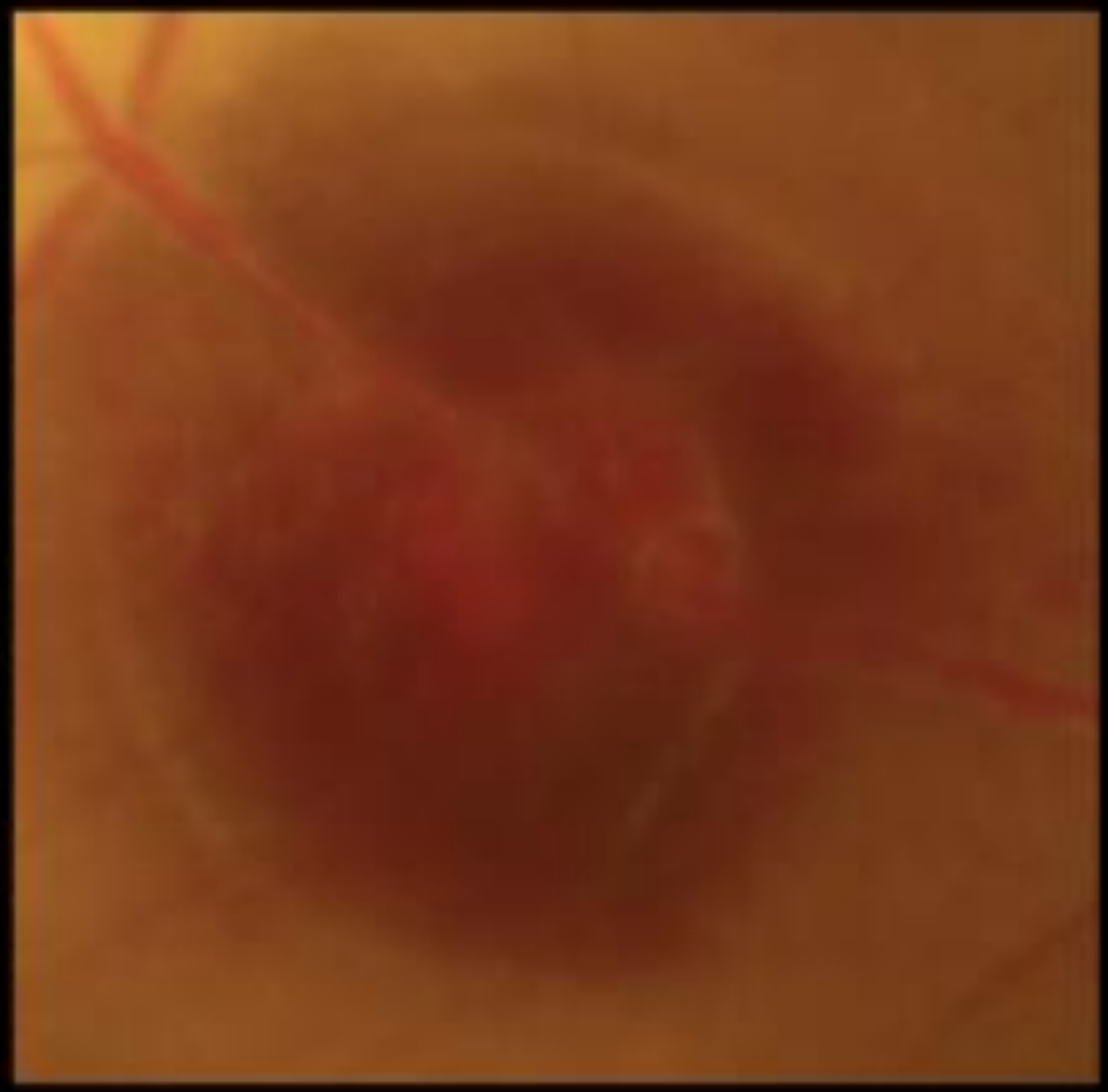
1. Detection

2. Monitoring

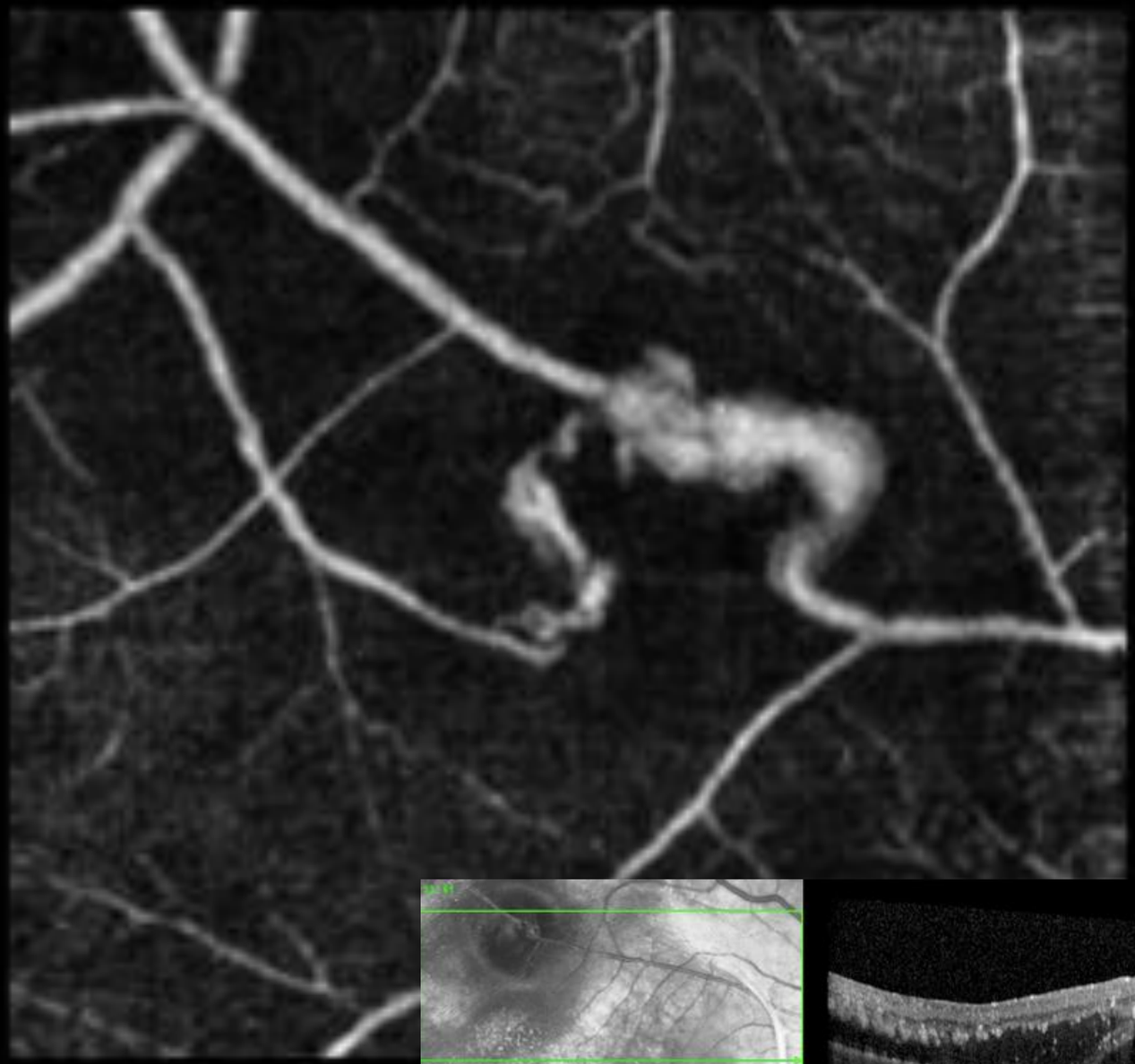
Lessons from other retinal vascular disease

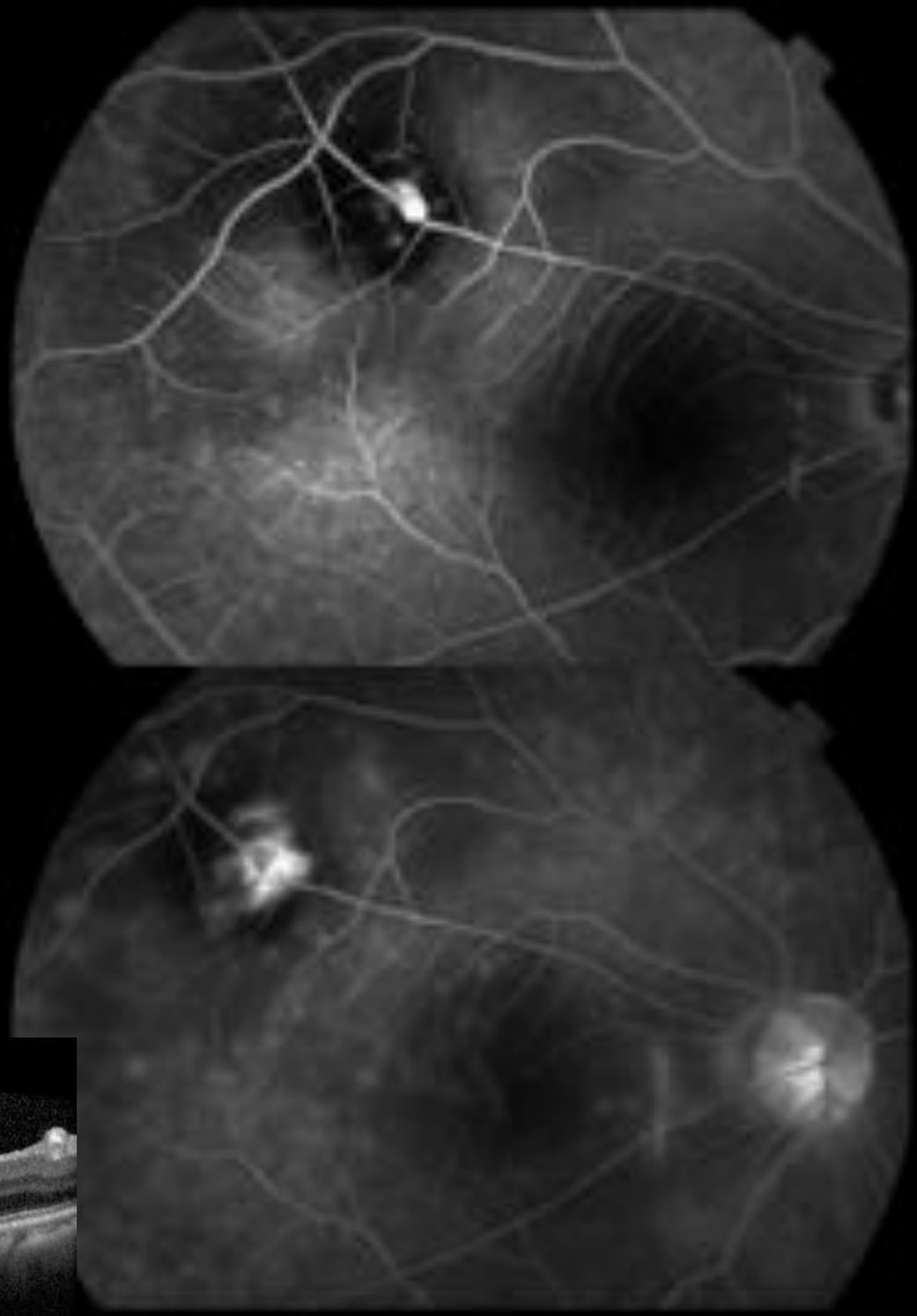
Macroaneurysm

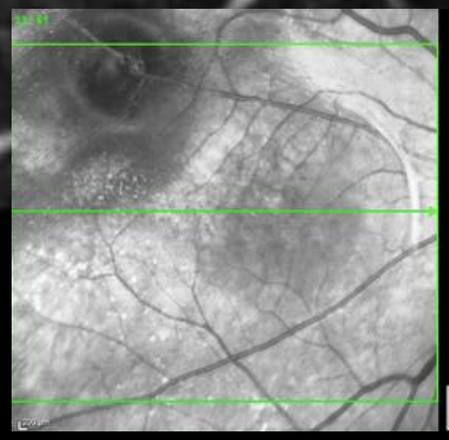


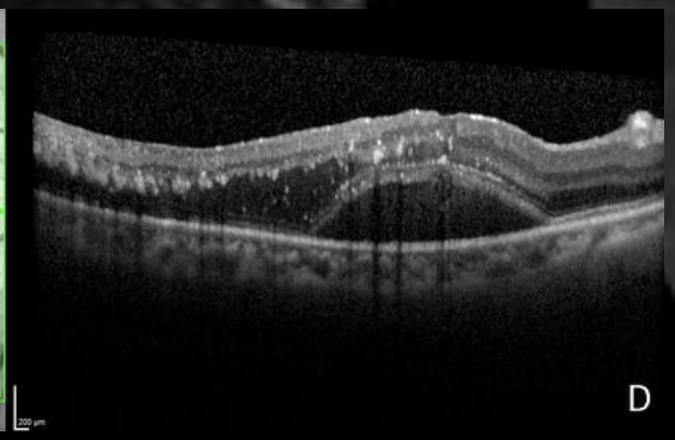


Macroaneurysm



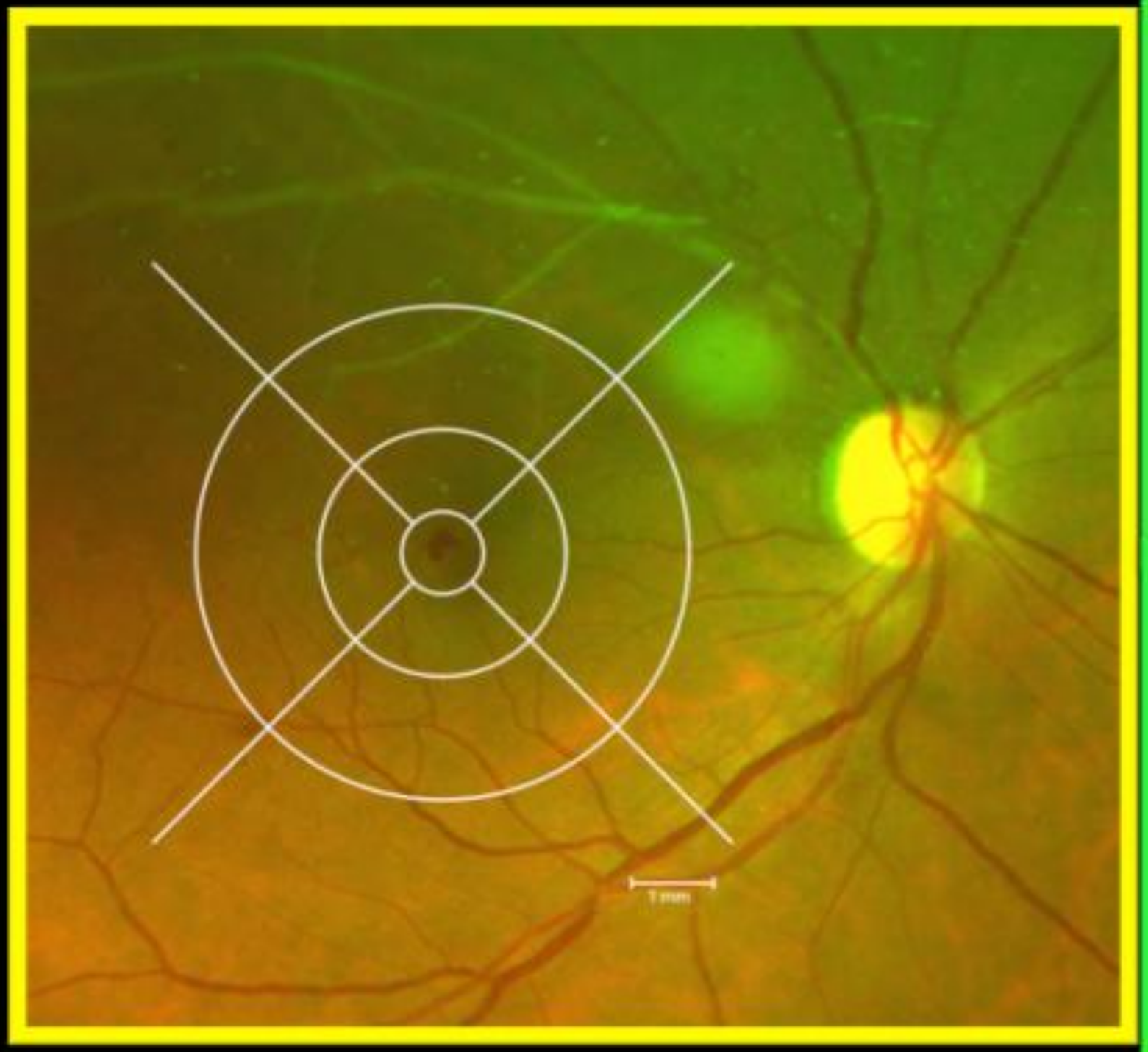


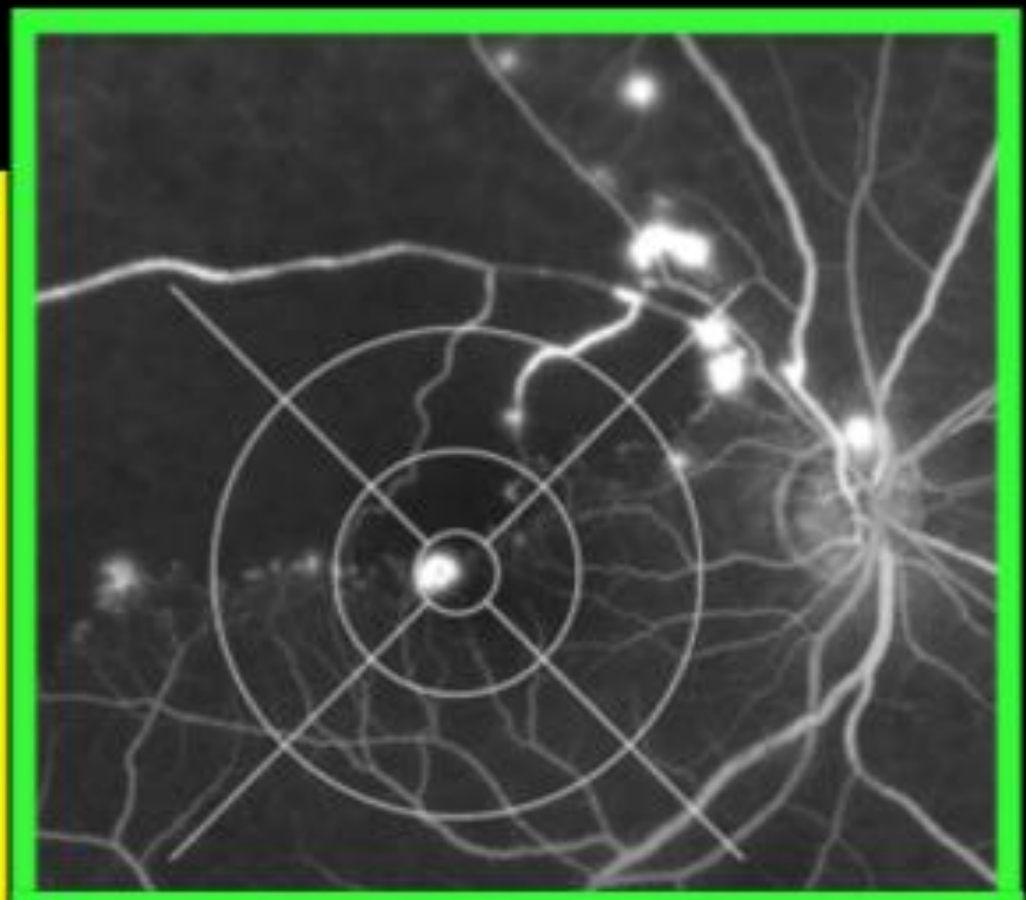


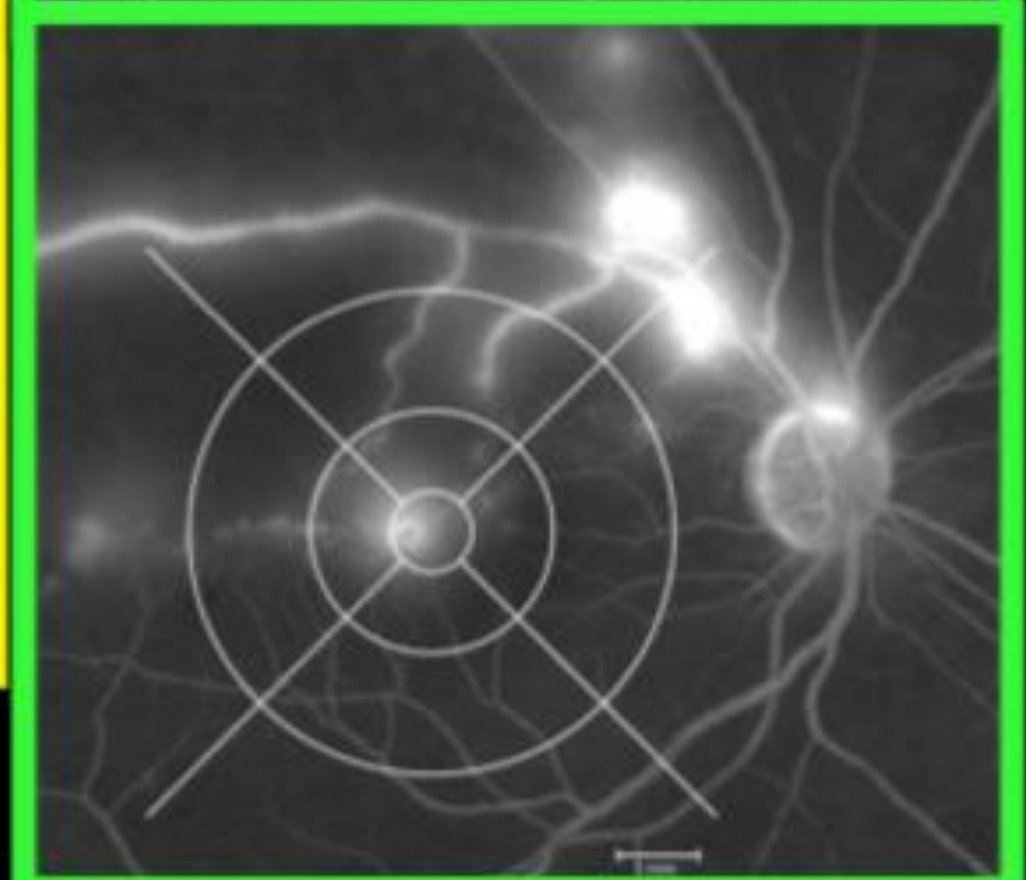


D

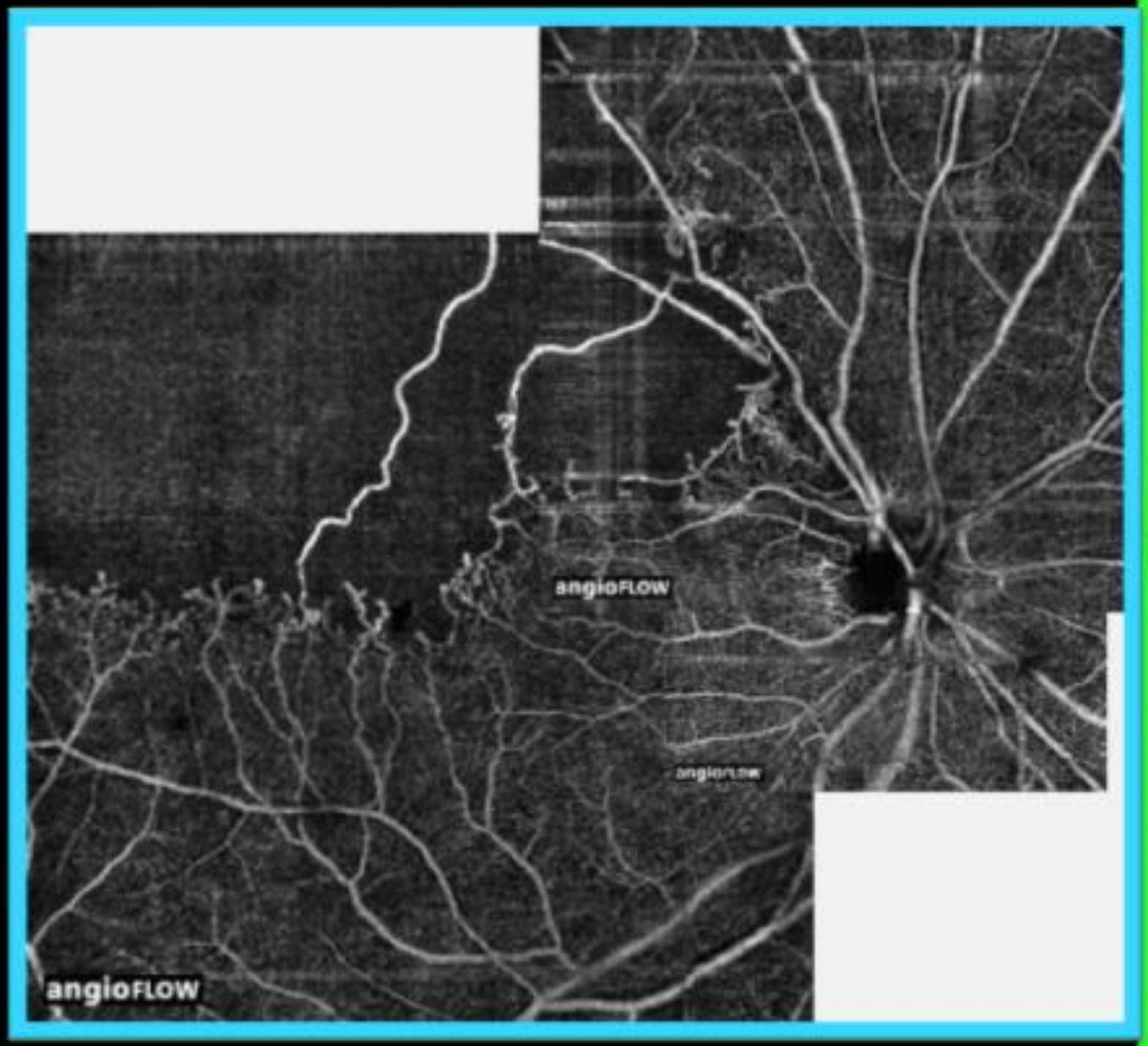
BRVO

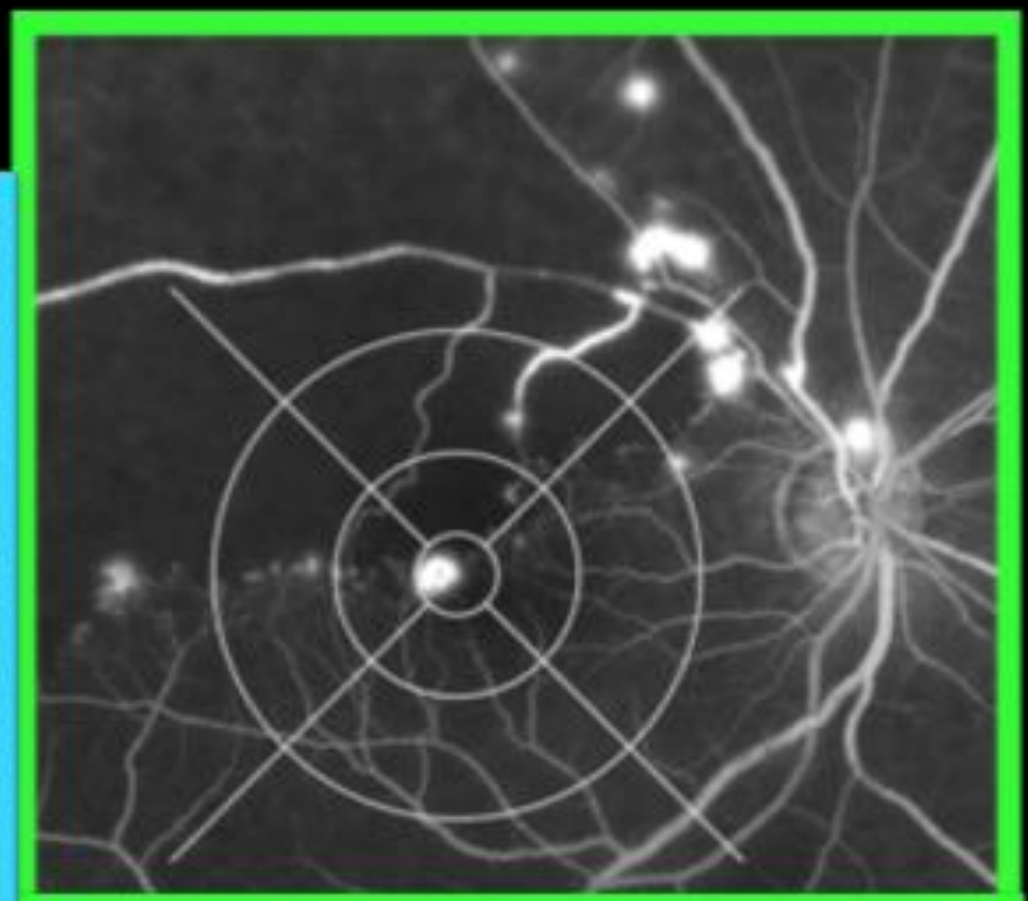


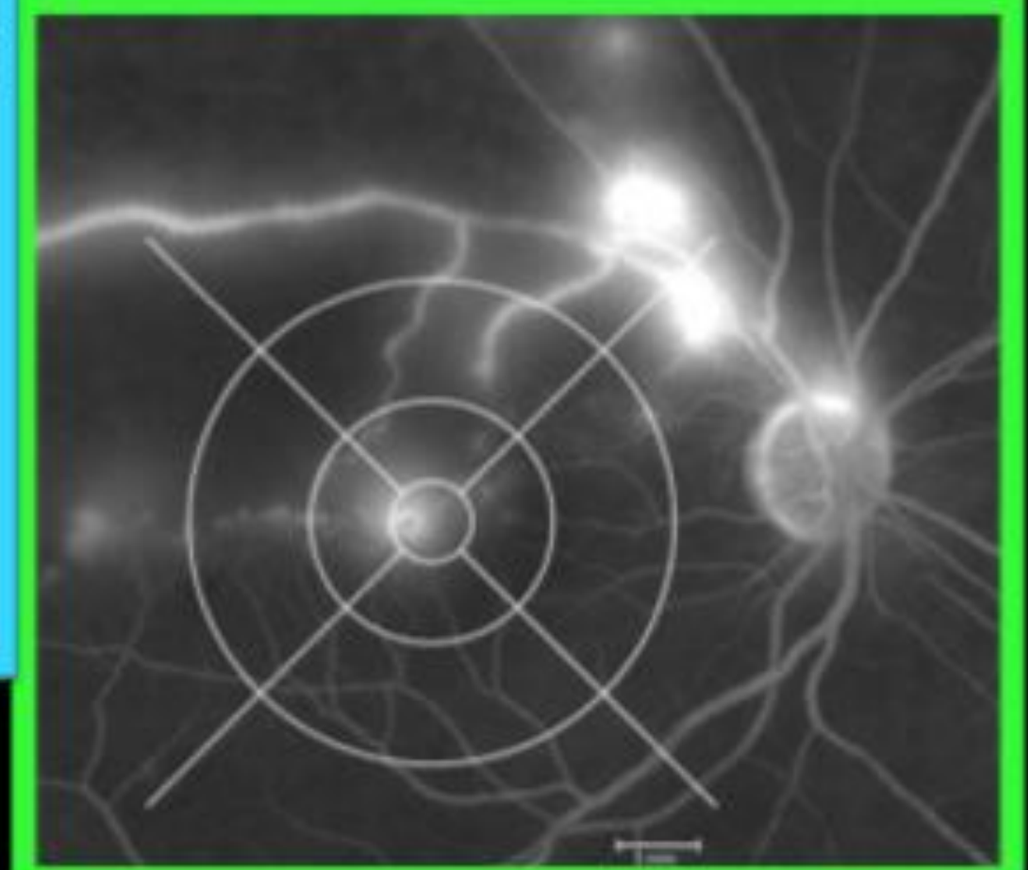




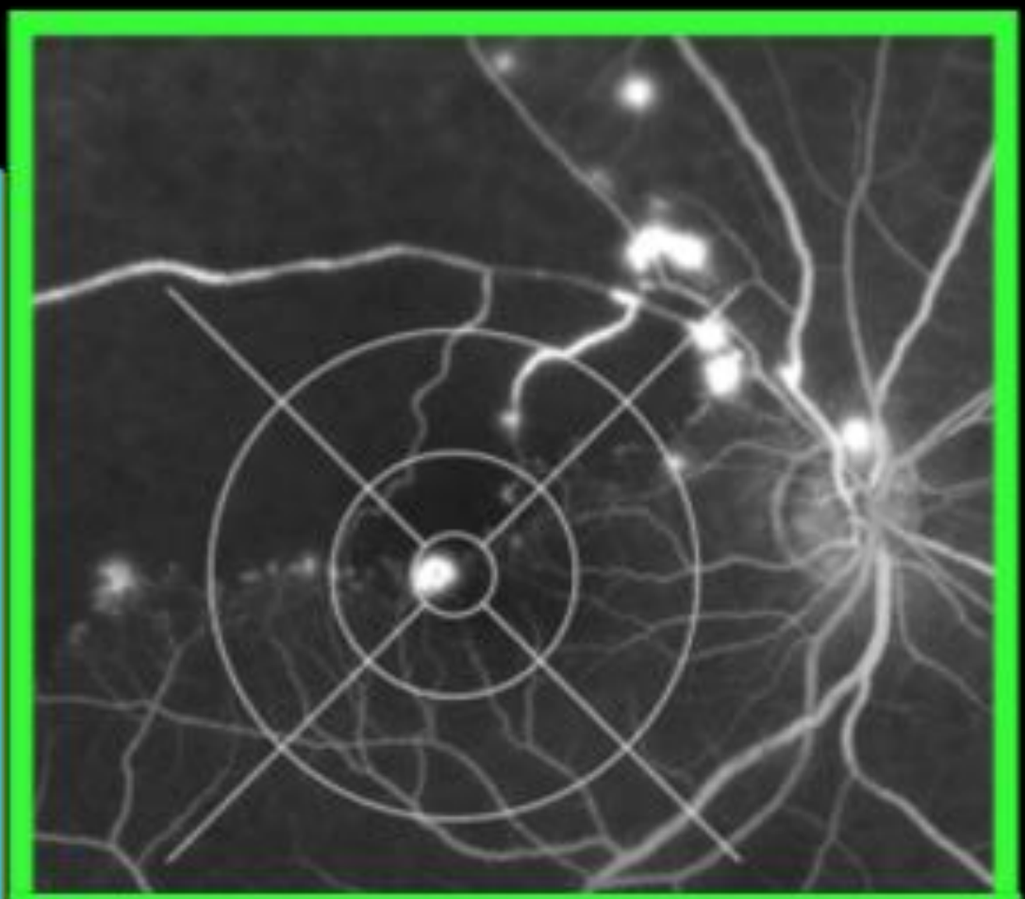
BRVO: no leak

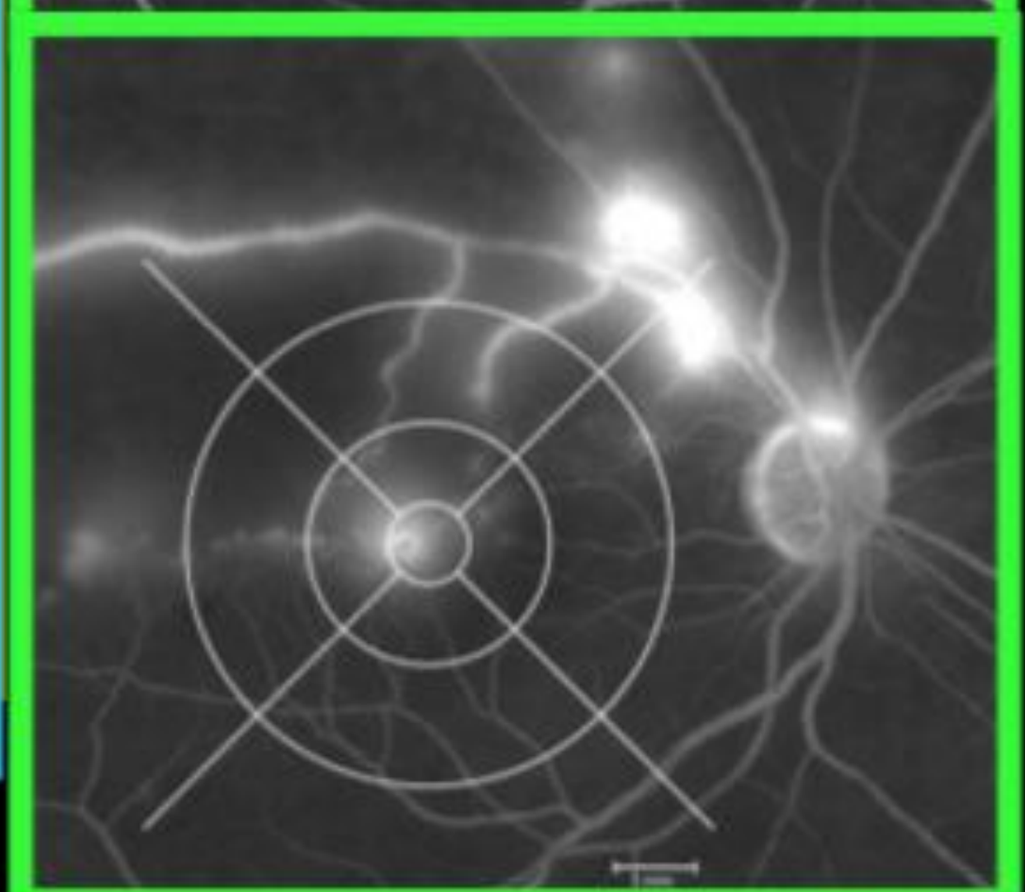






BRVO: clarity of FAZ

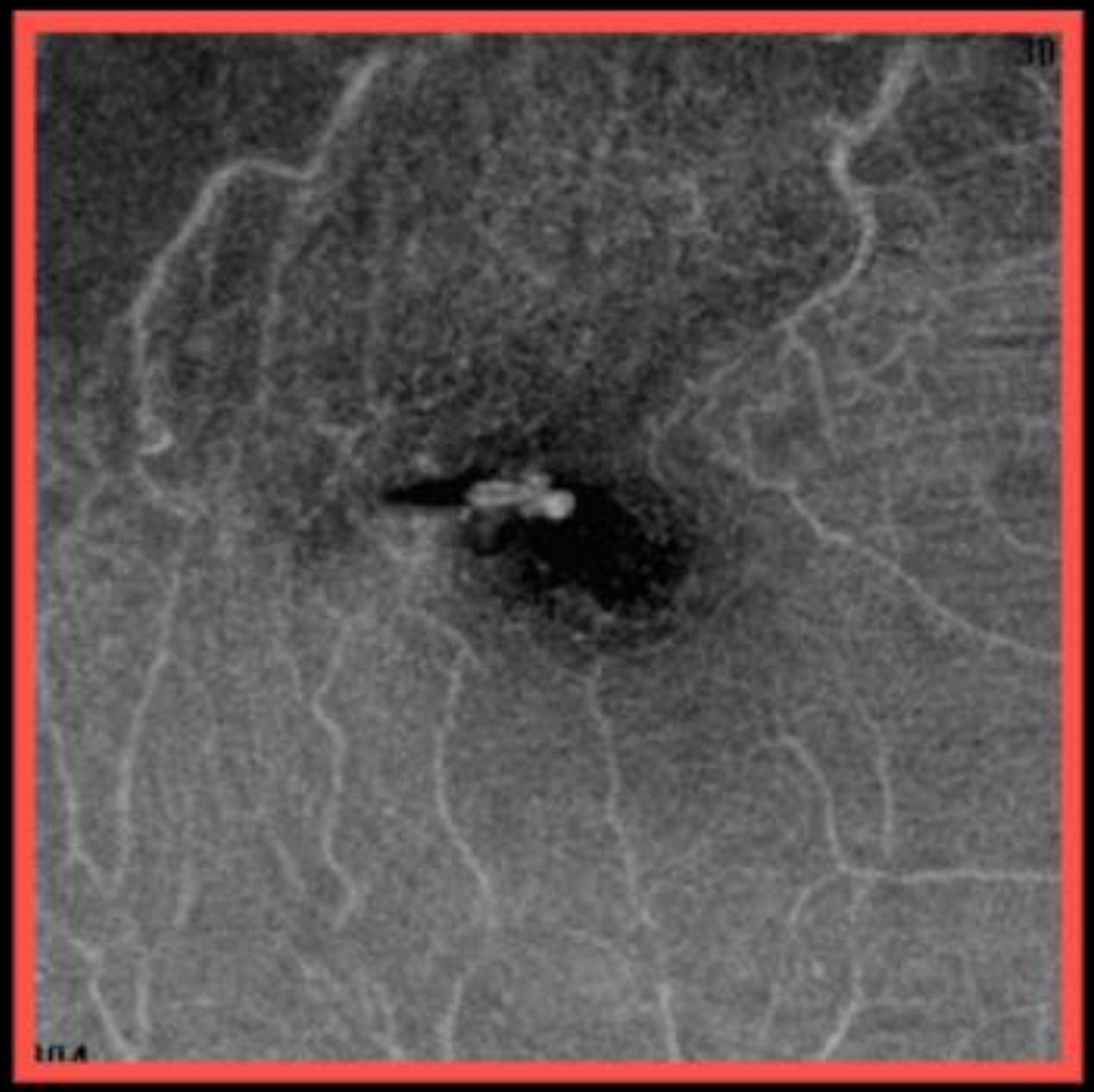




BRVO: Ghost vessels

OCTA

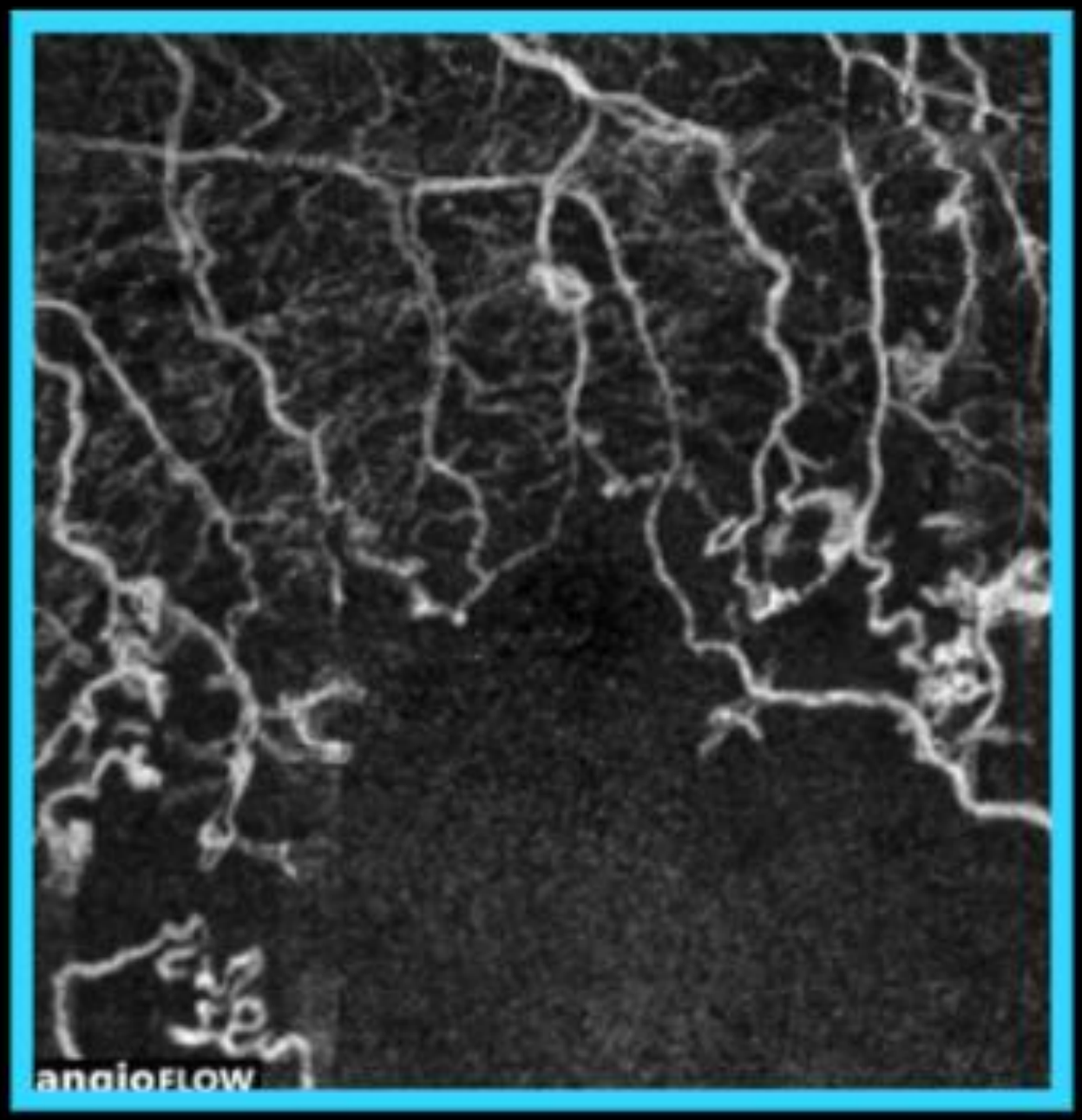
Function



Enface

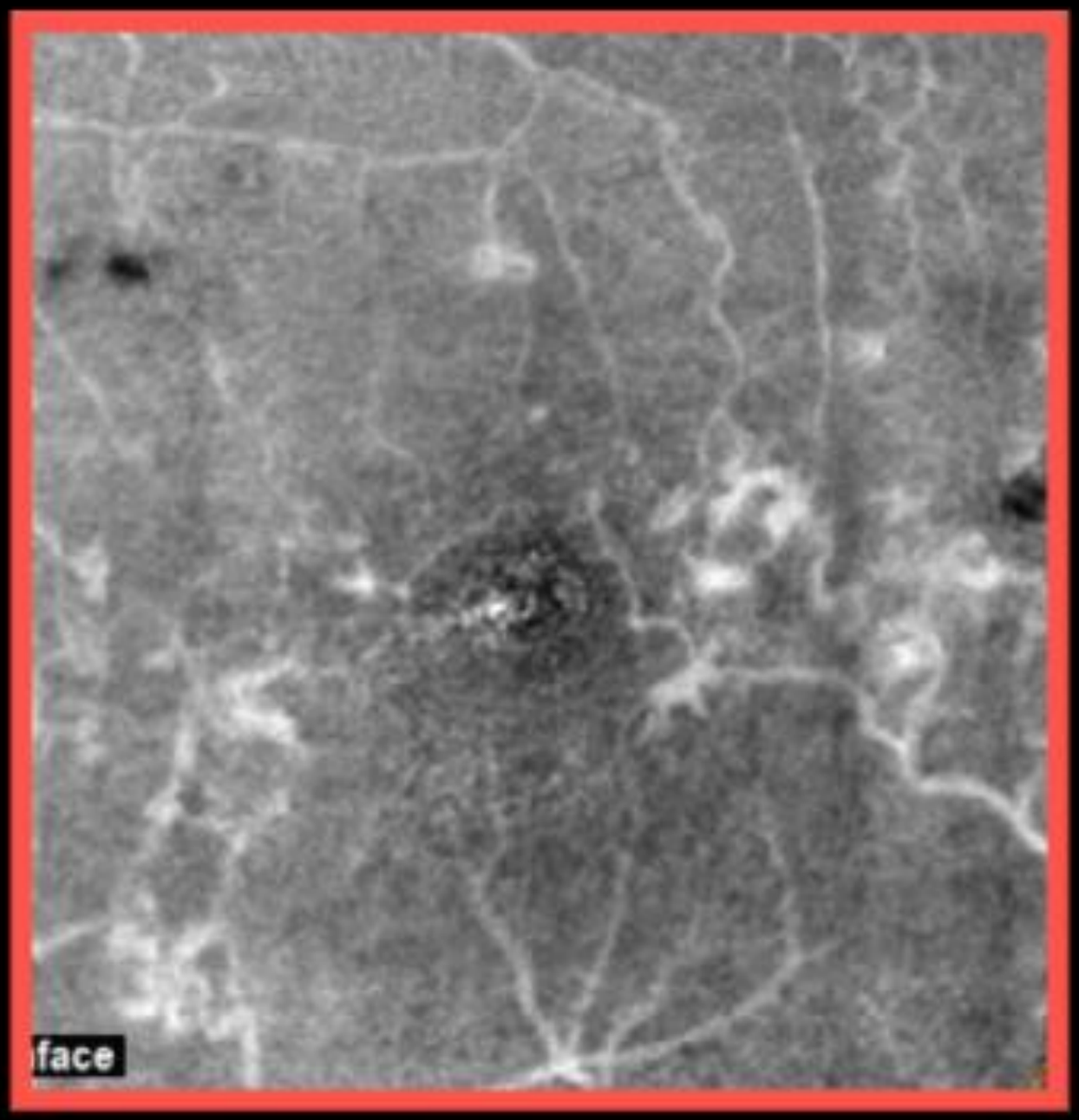
Structure

BRVO: Ghost vessels



OCTA

Function



Enface

Structure

Evaluation of Nonperfused Retinal Vessels in Ischemic Retinopathy

Michael B. Powner,[1,2] Dawn A. Sim,[1,3] Meidong Zhu,[4,5] João Nobre-Cardoso,[3] Ryan Jones,[1] Adil Syed,[4,6] Andrew A. Chang,[4,6] Pearse A. Keane,[1,3] Adnan Tufail,[1,3] Catherine A. Egan,[1,3] and Marcus Fruttiger[1]

[1]UCL Institute of Ophthalmology, University College London, London, United Kingdom
[2]Division of Optometry and Visual Science, School of Health Sciences, City University London, London, United Kingdom
[3]Moorfields Eye Hospital, London, United Kingdom
[4]Save Sight Institute, University of Sydney, Sydney, Australia
[5]Lions New South Wales Eye Bank, Sydney and Sydney Eye Hospital, Sydney, Australia
[6]Sydney Institute of Vision Science, Sydney, Australia

Correspondence: Marcus Fruttiger, UCL Institute of Ophthalmology, 11-43 Bath Street, London EC1V 9EL, UK;
m.fruttiger@ucl.ac.uk.

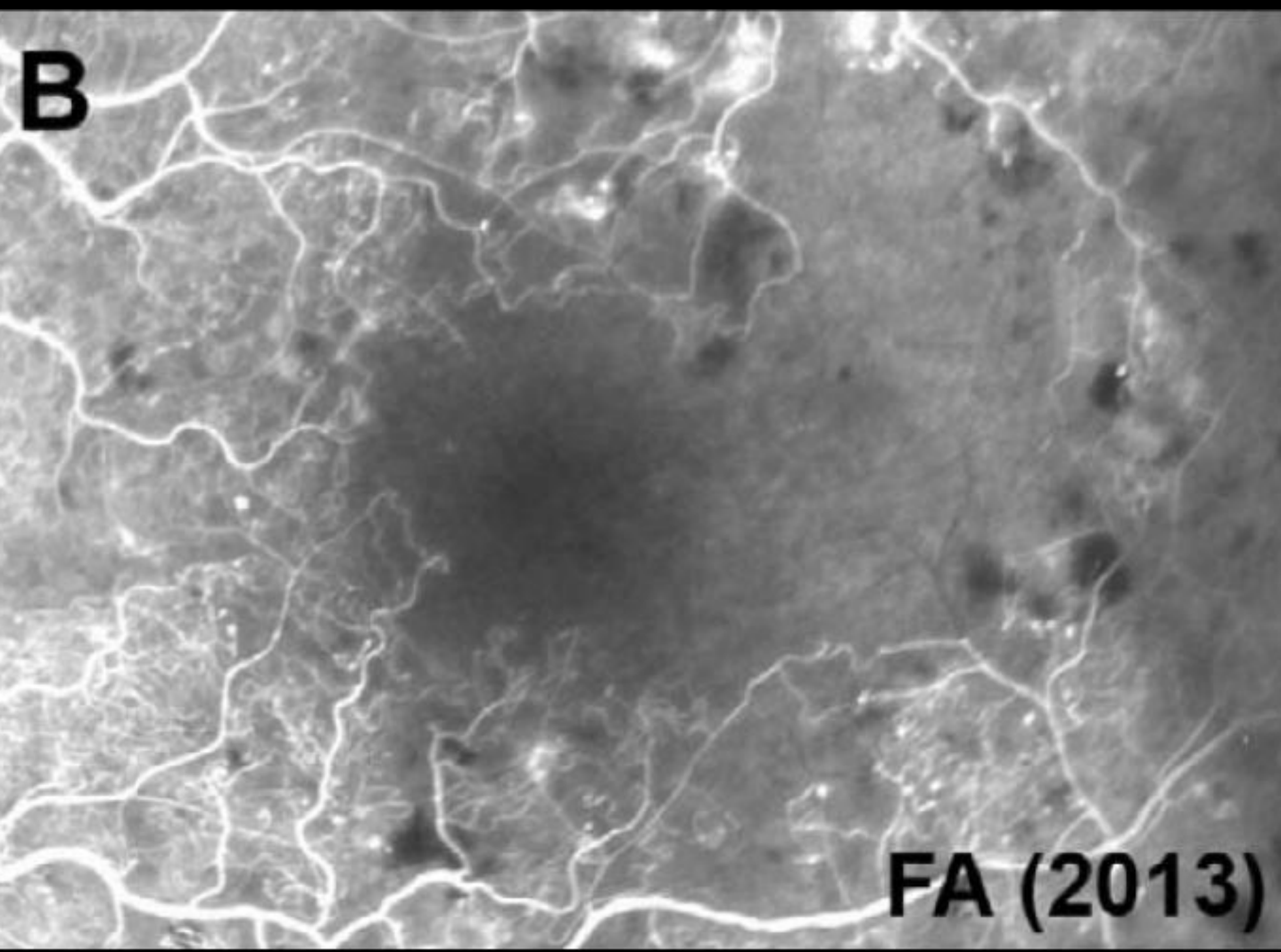
Submitted: May 26, 2016
Accepted: August 9, 2016

Citation: Powner MB, Sim DA, Zhu M, et al. Evaluation of nonperfused retinal vessels in ischemic retinopathy. *Invest Ophthalmol Vis Sci*. 2016;57:5031–5037. DOI:10.1167/iovs.16-20007

Purpose. Retinal ischemia has been traditionally assessed by fluorescein angiography, visualizing perfused vessels. However, this method does not provide any information about nonperfused vessels, and although it is often assumed that vessels in ischemic areas regress, we know little about how nonperfused retinal vessels change over time. Here, we aim to learn more about the long-term fate of nonperfused vessels in the retinal vasculature.

Methods. Optical coherence tomography (OCT) was used to visualize perfusion as well as structural properties of the retinal vasculature in patients suffering from retinal vascular occlusions. In addition, postmortem tissue from a patient with long standing (6 years) central retinal vein occlusion (CRVO) was investigated, using immunohistochemistry on whole-mount retina and paraffin sections to visualize blood vessel components.

Results. Comparing OCT angiography with enface OCT images revealed that in ischemic areas of the retina, nonperfused, larger vessels could be detected as hyperreflective structures in enface OCT images. Furthermore, analysis of a postmortem tissue sample from a CRVO patient with a large nonperfused region in the macula, revealed preservation of the basement membrane from all retinal vessels, including nonperfused, acellular vessels of all calibers.


B
FA (2013)

A

B

FA (2013)

C

Collagen IV + FA (2013)

dawn.sim@moorfields.nhs.uk