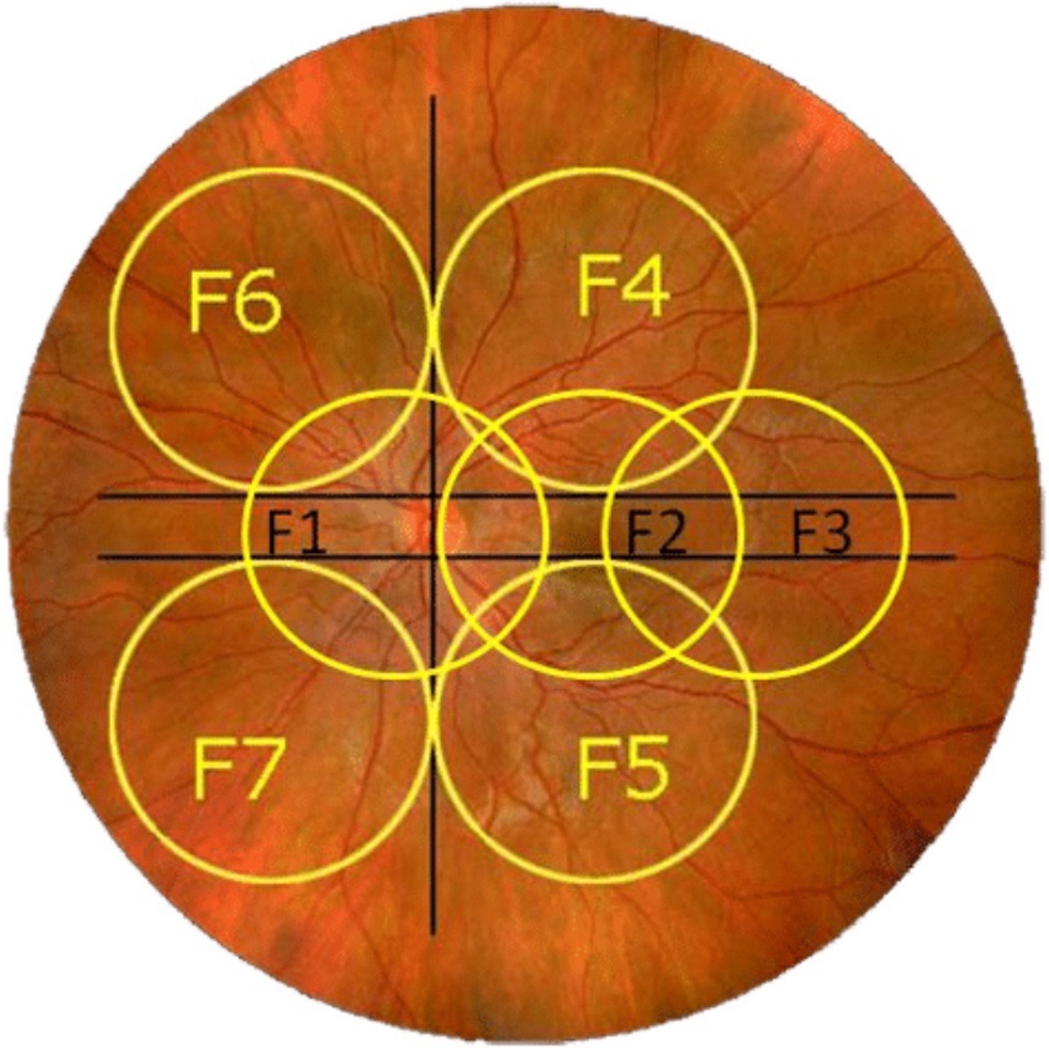
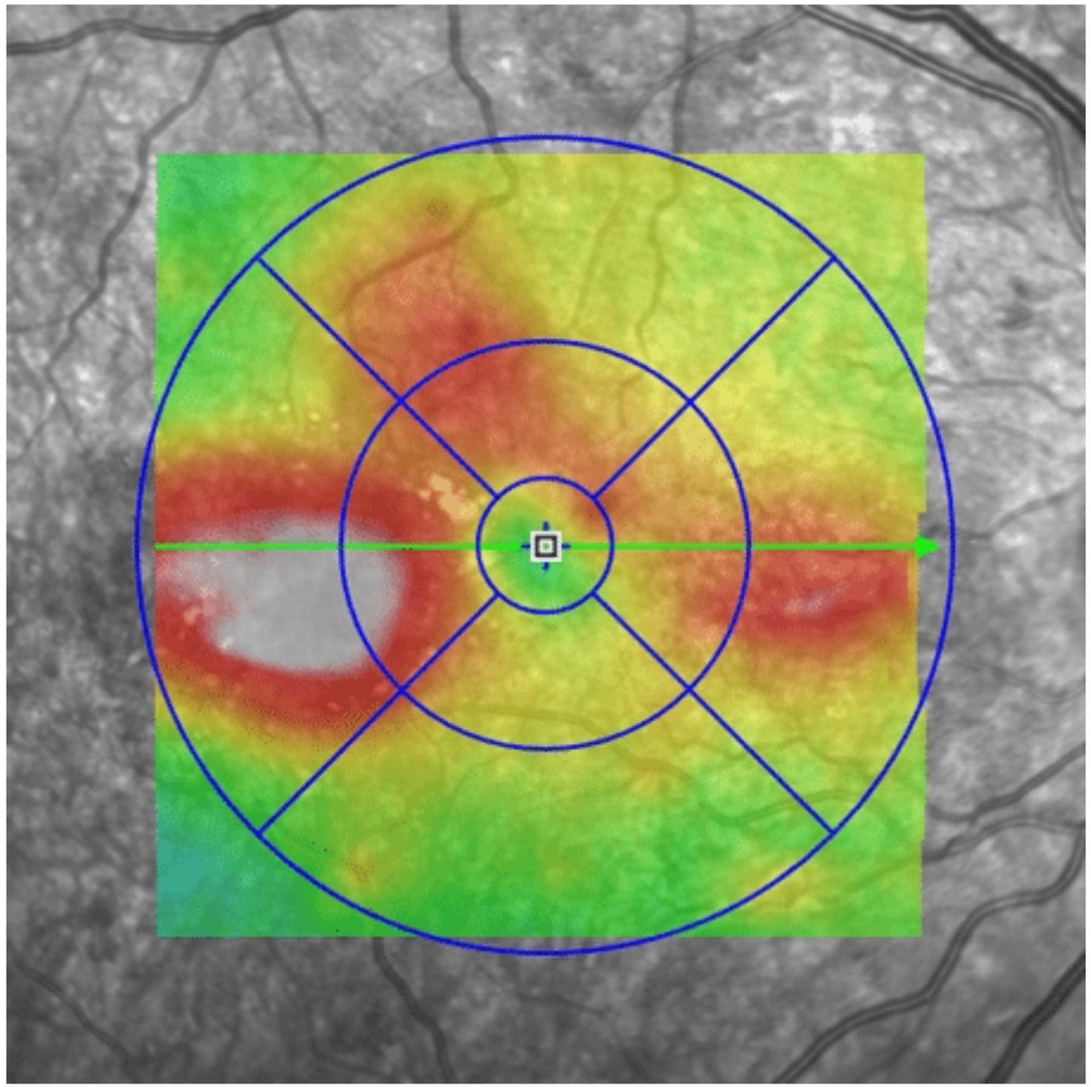
This course focuses on **recognising the key OCT signs** that can help manage patients with diabetic retinopathy in daily practice.



Fundus photograph



Macular thickness map

Identify the correct statement.

- ◯ Diabetes mellitus (DM) incidence is **increasing** worldwide
- ◯ Diabetes mellitus (DM) incidence is **decreasing** worldwide

SUBMIT

What is the leading cause of vision loss in western countries, among working-aged groups?

- ◯ Macular degeneration
- ◯ Glaucoma
- ◯ Diabetic retinopathy

SUBMIT

What is the main cause of vision loss in diabetic retinopathy (DR).

- ○ Proliferative diabetic retinopathy (PDR)
- ○ Diabetic macular edema (DME)

SUBMIT

Recap

- Diabetes mellitus (DM) incidence is **increasing** worldwide
- Diabetic retinopathy (DR) is the leading cause of vision loss in western countries among working-aged groups
- Diabetic macular edema (DME) is the main cause (by far) of vision loss in diabetic retinopathy (DR)

Course overview

This course will examine:

- What is diabetic macular edema (DME)?
- When to perform an OCT for patients with diabetes mellitus (DM)?
- What to expect from OCT images?

What is DME?

DME is defined by the presence of either:

- **Retinal thickening** *and/or*
- **Retinal exudates**

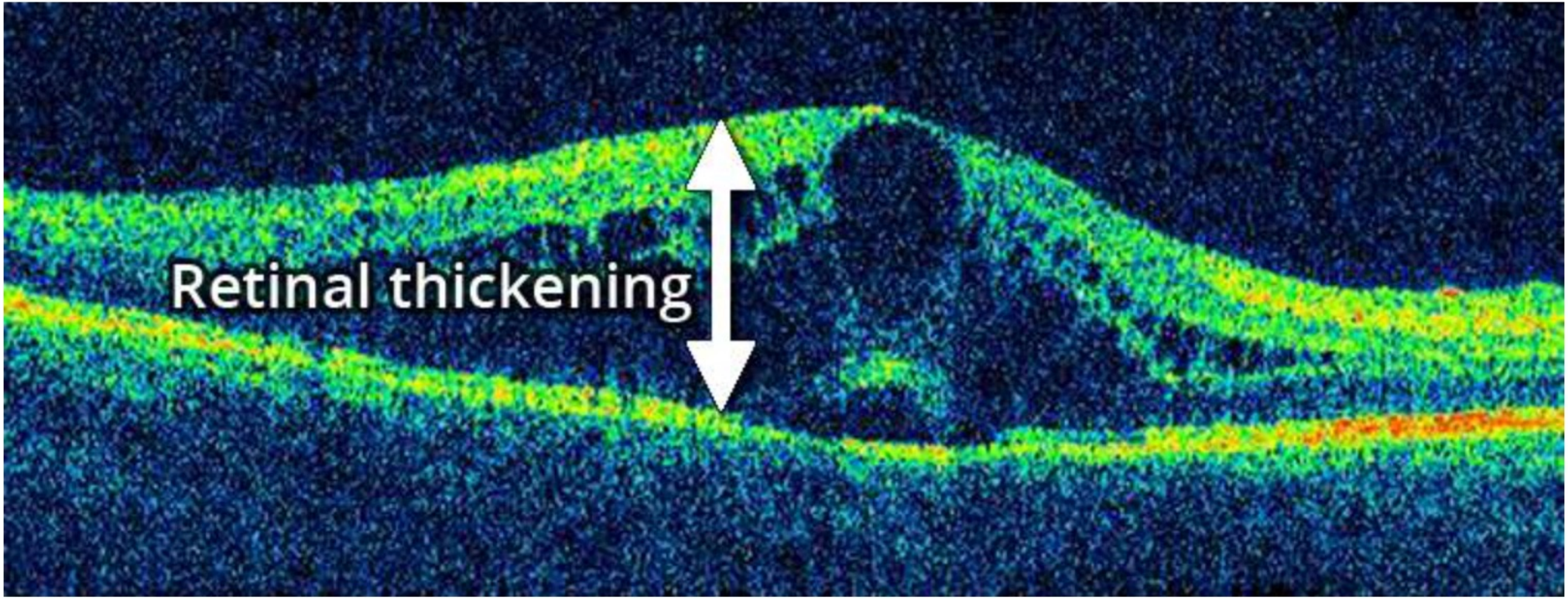
Retinal thickening is mostly seen on...

Click to flip

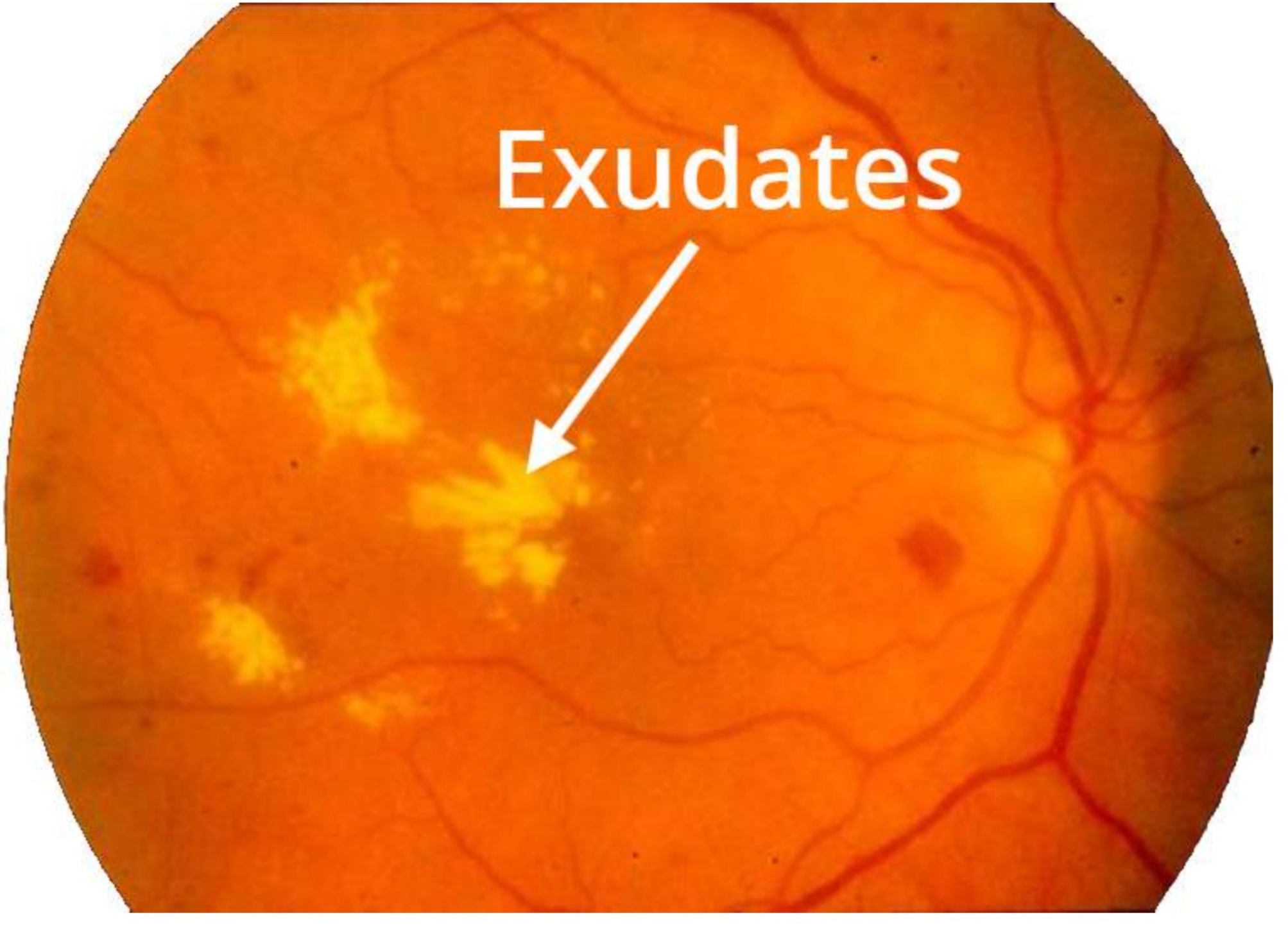
Retinal exudates are mostly seen on...

... **OCT**

... **fundus photography**



Retinal thickening is mostly seen on OCT



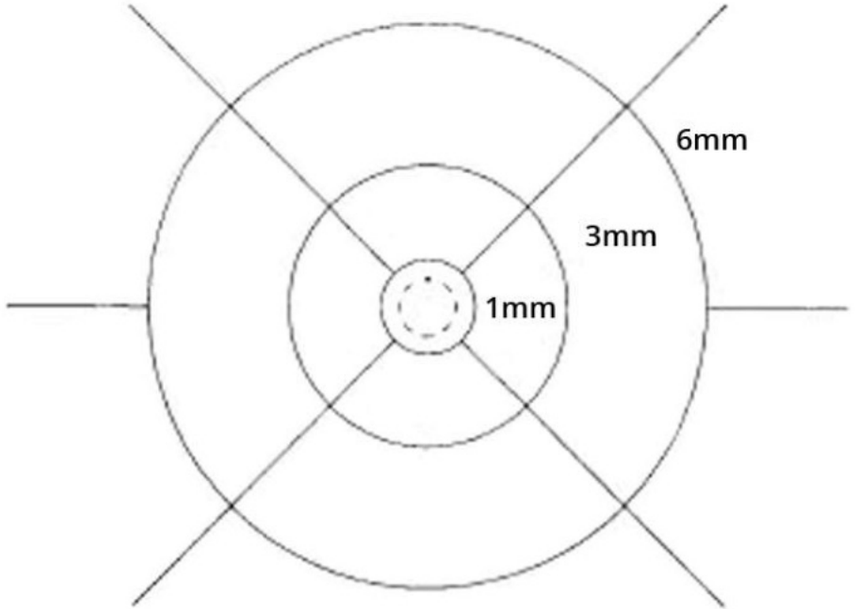
Retinal exudates are mostly seen on fundus photography

Which of the following is the key to determining DME severity?

- ◯ Duration of DME
- ◯ Location of DME
- ◯ Size of DME

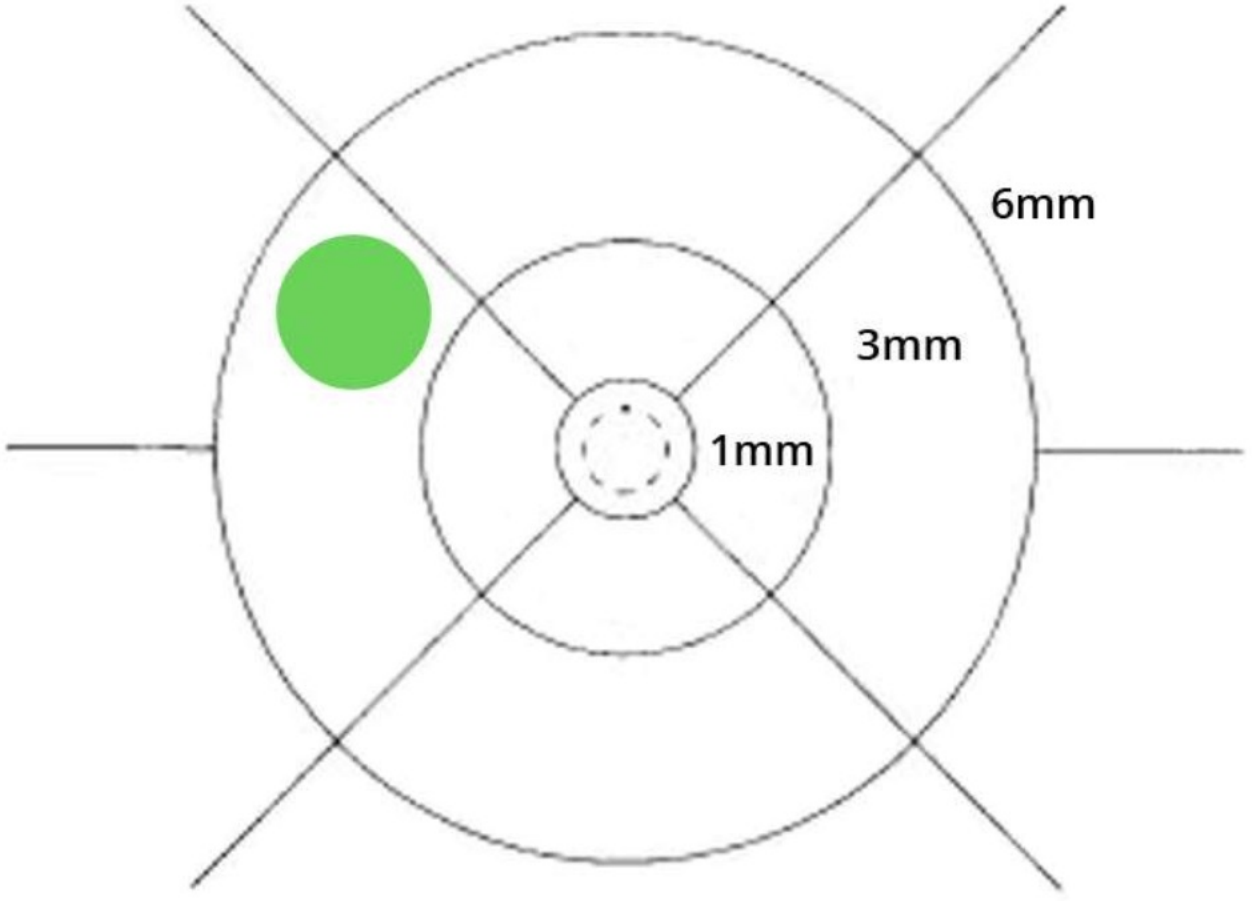
SUBMIT

So, **DME severity** is determined by DME **location**.

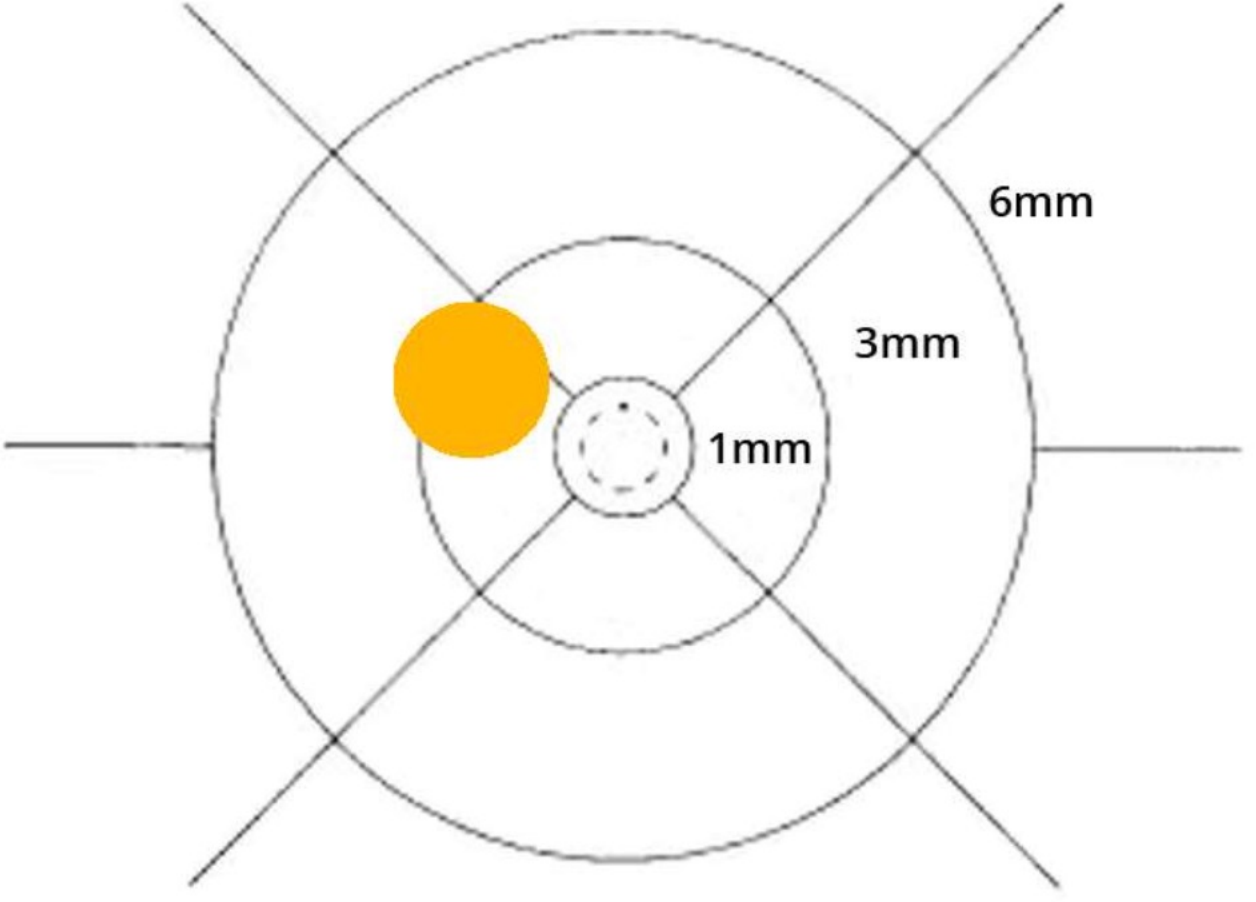


Thickness mapping (distance from fovea)

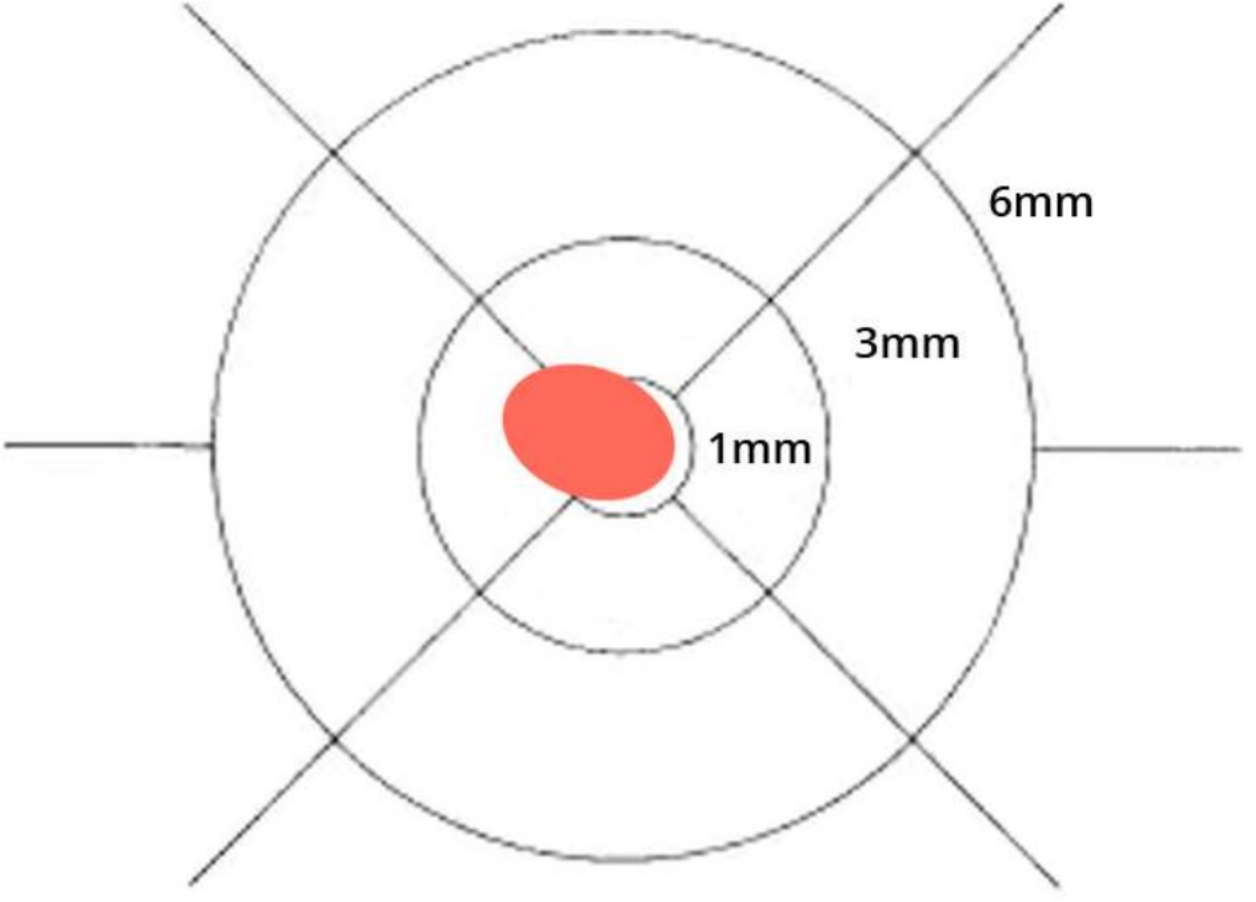
Mild DME is when the DME is remote from the fovea.



Moderate DME is when the DME is "threatening" the fovea.

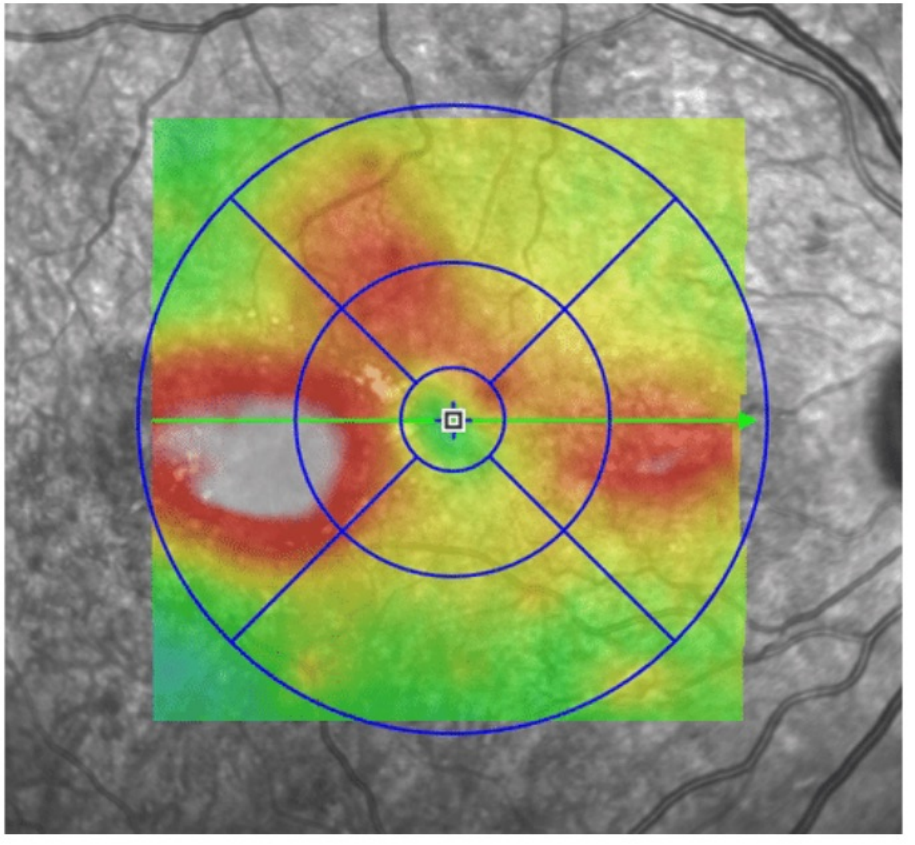


Severe DME is when the DME involves the fovea.



MILD DME	MODERATE DME	SEVERE DME	OCT MACULAR THICKNESS MAP

OCT macular thickness mapping clearly shows the thickening of the retina. This is, therefore, the best examination for identifying the location of the DME.



What was DME in the past?

What was diabetic macular edema (DME) called in the past?

- ○ Proliferative diabetic retinopathy (PDR)
- ○ Clinically significant macular edema (CSME)
- ○ Cystoid macular edema (CME)

The Early Treatment of Diabetic Retinopathy Study (ETDRS) defined **3 severity levels** for diabetic macular edema:

- Diabetic macular edema apparently **absent**
- Diabetic macular edema apparently **present**
- **Clinically significant macular edema**

TABLE A6-2 DIABETIC MACULAR EDEMA DISEASE DEFINITIONS IN THE EARLY TREATMENT OF DIABETIC RETINOPATHY STUDY

Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy
Diabetic macular edema apparently absent	No apparent retinal thickening or hard exudates in posterior pole
Diabetic macular edema apparently present	Thickening of retina within one disc diameter of the center of the macula; and/or hard exudates ≥ standard photograph 3* in a standard 30° photographic field centered on the macula (field 2), with some hard exudates within one disc diameter of the center of the macula
Clinically significant macular edema	Retinal thickening at or within 500 µm of the center of the macula; and/or hard exudates at or within 500 µm of the center of the macula, if associated with thickening of the adjacent retina; and/or a zone or zones of retinal thickening one disc area in size at least part of which was within one disc diameter of the center

Adapted with permission from the Early Treatment Diabetic Retinopathy Study Research Group. Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics: ETDRS report number 7. Ophthalmology 1991;98:742.

* Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs--an extension of the modified Airlie House classification: ETDRS report number 10. Ophthalmology 1991;98:786-806.

DME severity levels as defined by the ETDRS (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

Clinically Significant Macular Oedema

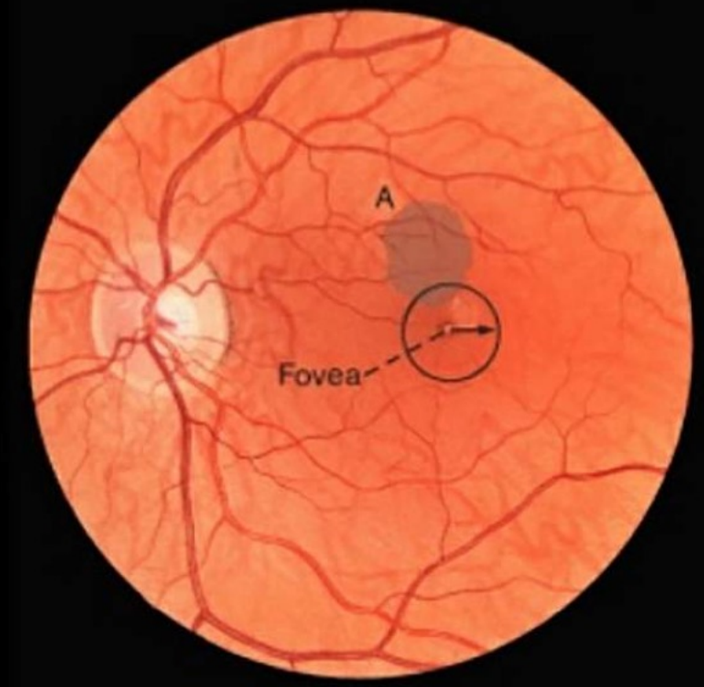


Image A: Retinal oedema within 500 µm of centre of fovea.

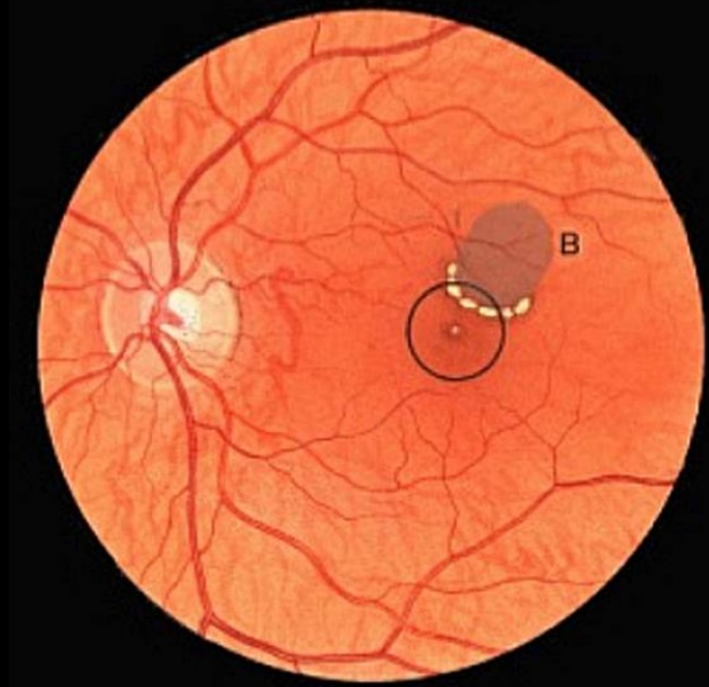


Image B: Hard exudates within 500 µm of centre of fovea with adjacent oedema which may be outside 500 µm limit.

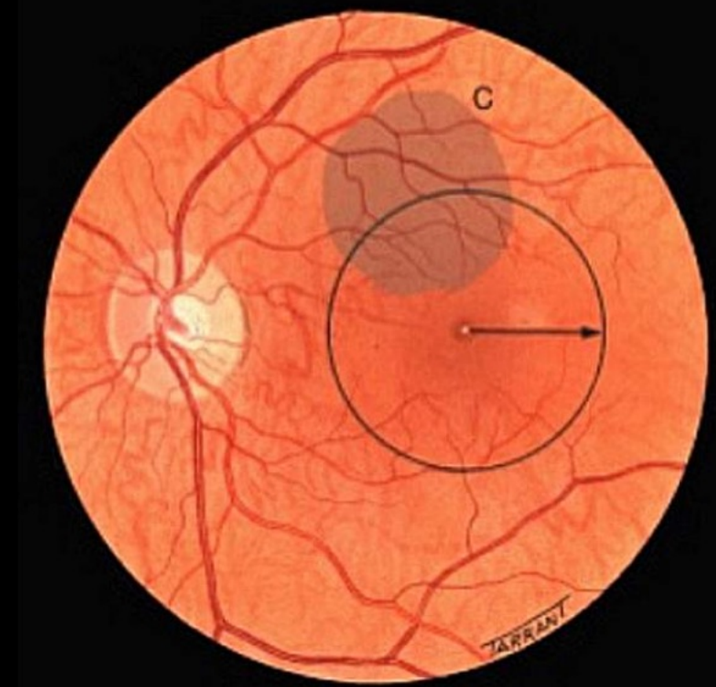


Image C: Retinal oedema one disc area or larger any part of which is within one disc diameter (1500 µm) of centre of fovea.

In these 3 cases above:

- **Image A and B show an involvement of the centre**, either by thickening or by exudates.
- **Image C** shows a thickening which **does not involve the centre**.

In the past, it was at times difficult to actually figure out what was clinically significant macular edema using the ETDRS definition.

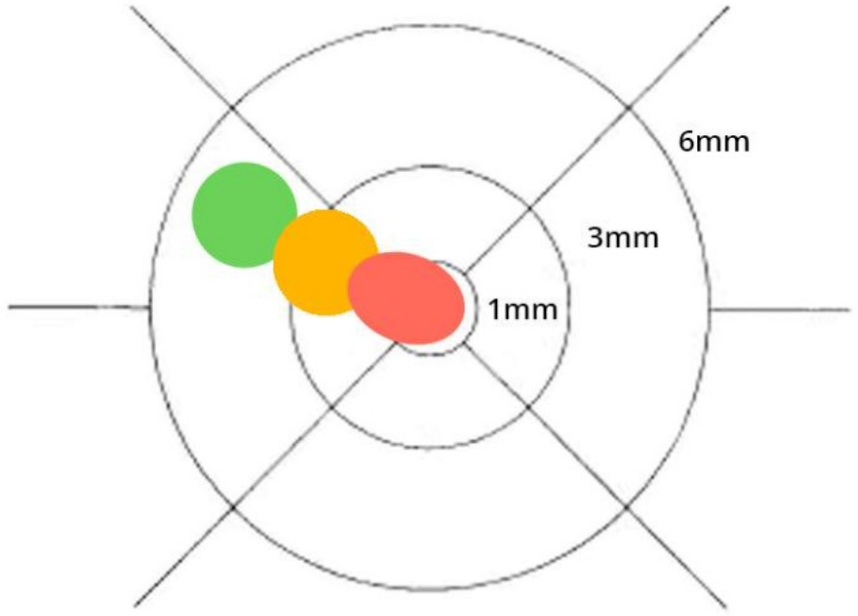
Identify the correct statement.

- The ETDRS definition is still used in most practices today.
- Nowadays, the ETDRS definition is no longer used in most practices. The main focus is now on the involvement of the centre.

Nowadays, the **ETDRS definition is no longer used in most practices**. The main focus is now on the **involvement of the centre**.

Disease severity scales

Nowadays, international classifications use the **location** of the DME to assess the **severity**.



Location of DME

Proposed International Classification (Wilkinson et al., 2003)

Proposed International Classification (Wilkinson et al., 2003)

TABLE 2 INTERNATIONAL CLINICAL DIABETIC MACULAR EDEMA DISEASE SEVERITY SCALE

Proposed Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy
Diabetic macular edema apparently absent	No apparent retinal thickening or hard exudates in posterior pole
Diabetic macular edema apparently present	Some apparent retinal thickening or hard exudates in posterior pole
If diabetic macular edema is present, it can be categorized as follows:	
Proposed Disease Severity Level	**Findings Observable upon Dilated Ophthalmoscopy***
Diabetic macular edema present	• Mild diabetic macular edema: some retinal thickening or hard exudates in posterior pole but distant from the center of the macula • Moderate diabetic macular edema: retinal thickening or hard exudates approaching the center of the macula but not involving the center • Severe diabetic macular edema: retinal thickening or hard exudates involving the center of the macula

Reproduced with permission from Wilkinson CP, Ferris FL III, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003;110:1680.

* Hard exudates are a sign of current or previous macular edema. Diabetic macular edema is defined as retinal thickening; this requires a three-dimensional assessment that is best performed by dilated examination using slit-lamp biomicroscopy and/or stereoscopic fundus photography. Optical coherence tomography may supplement the fundus evaluation for determining the presence of diabetic macular edema.

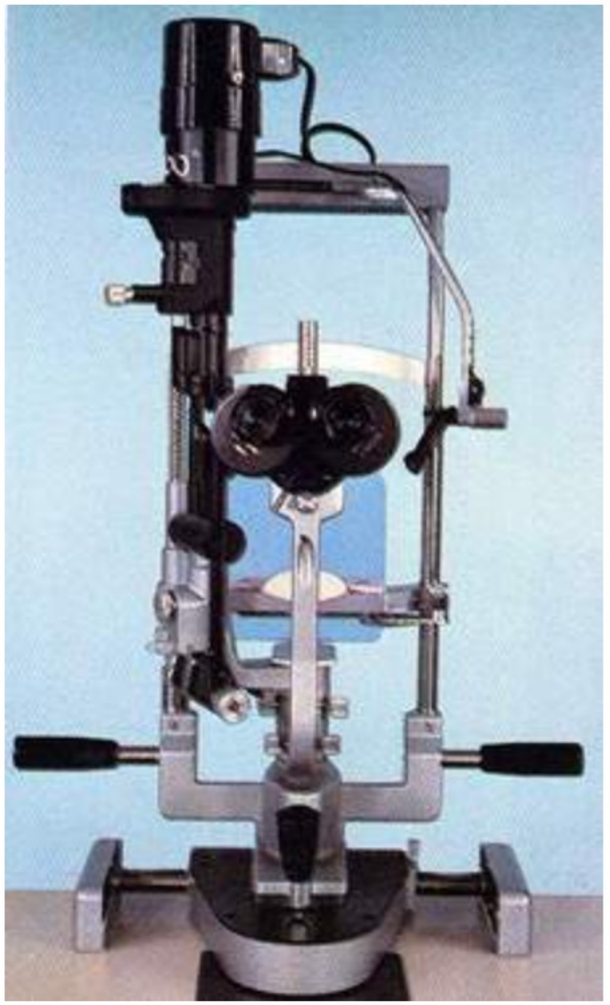
Proposed International DME severity scale by Wilkinson et al., 2003 (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

Imaging Examination Recommendations

(Wilkinson et al., 2003)

All examinations in the above table are initially performed using **slit-lamp biomicroscopy and/or fundus photography**.

The recommendation is to **perform OCT only if** the thickening or exudates cannot be assessed using funduscopy and slit-lamp examination.



Slit Lamp

DME needs to be classified due to the fact that clinically significant macular edema (CSME) leads to vision loss, and when therefore correctly identified, laser treatment can decrease the rate of vision loss in these patients.

Types of DME

The table below, from the ETDRS, shows the 2 types of patients with clinically significant macular edema (CSME):

- patients **with centre-involving** macular edema
- patients **without centre-involving** macular edema

TABLE A4-2 VISUAL OUTCOME FOR LASER PHOTOCOAGULATION TREATMENT FROM THE EARLY TREATMENT DIABETIC RETINOPATHY STUDY

Extent of Macular Edema	Duration of Follow-up (Years)	Control Patients (% with Visual Loss)	Treated Patients (% with Visual Loss)
CSME (center of macula not involved)	1	8	1
	2	16	6
	3	22	13
CSME (center of macula involved)	1	13	8
	2	24	9
	3	33	14

CSME = clinically significant macular edema

NOTE: Visual loss was defined as at least doubling of the visual angle.

ETDRS Visual Outcome for Laser Photocoagulation (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

The results in the table show that the **worst prognosis is for patients with centre-involving macular edema**.

However, note that **patients with centre involvement have a greater benefit from laser treatment** compared to patients with no centre involvement.

So, nowadays, the simple classification of DME is:

'Centre-Involving DME'

versus

'Non Centre-Involving DME'

You should use this simple classification in daily practice to assess patients and to decide the best treatment approach.

Treatment for centre-involving DME

Anti-VEGF injections are the main treatment today for centre-involving DME.

Anti-VEGF injections for centre-involving DME

When to perform an OCT?

Recommendations for when to perform an OCT in diabetic patients (AAO)

The 2017 recommendations from the American Academy of Ophthalmology (AAO), for the use of OCT for diabetic retinopathy, are shown in the table below.

TABLE 4 USE OF OPTICAL COHERENCE TOMOGRAPHY FOR DIABETIC RETINOPATHY

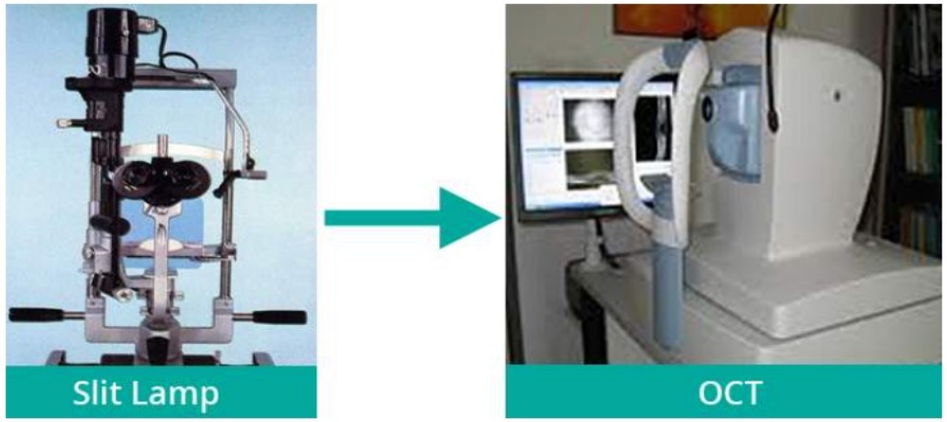
Situation	Usually	Occasionally	Never
To evaluate unexplained visual acuity loss	•		
To identify areas of vitreomacular traction	•		
To evaluate patients with difficult and/or questionable examinations for DME	•		
To investigate other causes of macular swelling		•	
To screen a patient with no or minimal diabetic retinopathy			•

DME = diabetic macular edema

Use of OCT for Diabetic Retinopathy (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

2017 AAO recommendations:

- OCT is not required when screening a patient with no or minimal involvement in the retina
- Use OCT if there is difficulty assessing the thickness or the DME



Only use OCT if having difficulty assessing thickness or DME

Pierre-Raphaël ROTHSCHILD (course editor) recommends that you:

Do an OCT for every patient,
as it is often quite difficult to
assess the retina with
fundus/biomicroscopy alone

When to perform FA?

Identify the correct statement.

- Fluorescein angiography is never useful for diabetic retinopathy.
- The use of fluorescein angiography for diabetic retinopathy is very important, and must be considered in terms of when to combine with OCT imaging.

The use of fluorescein angiography for diabetic retinopathy is very important and must be considered in terms of when to combine with OCT imaging.

AAO Recommendations for when to use FA in diabetic patients

The 2017 recommendations from the American Academy of Ophthalmology (AAO), for the use of fluorescein angiography (FA) for diabetic retinopathy, are shown in the table below.

TABLE 5 USE OF FLUORESCEIN ANGIOGRAPHY FOR DIABETIC RETINOPATHY

Situation	Usually	Occasionally	Never
To guide laser treatment of CSME	•		
To evaluate unexplained visual loss	•		
To identify suspected but clinically obscure retinal neovascularization	•		
To identify areas of vitreomacular traction		•	
To rule out other causes of macular swelling		•	
To identify large areas of capillary nonperfusion		•	
To evaluate patients with difficult and/or questionable examinations for DME		•	
To screen a patient with no or minimal diabetic retinopathy			•

CSME = clinically significant macular edema; DME = diabetic macular edema

Use of FA for Diabetic Retinopathy (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

The AAO (2017) recommends that fluorescein angiography (FA) may be used in combination with OCT to:

- Guide laser treatment
- Rule out other causes of macular swelling
- Assess macular ischemia / identify large areas of capillary nonperfusion

OCT and FA for patients with DM

Pierre-Raphaël ROTHSCHILD (course editor)

recommends and uses the following approach in his daily practice:

Pierre-Raphaël ROTHSCHILD, MD, PhD

1. Always perform an OCT

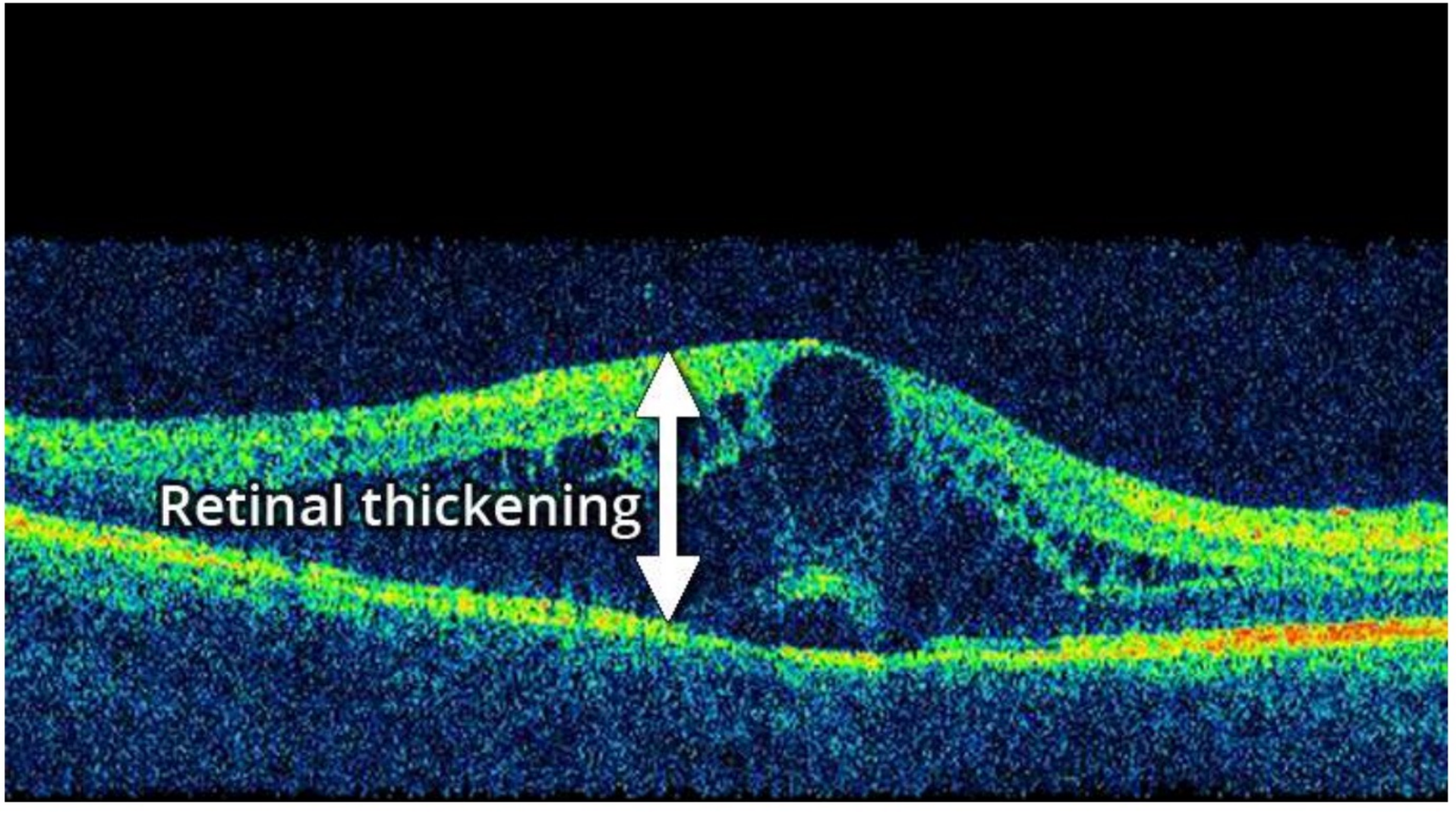
2. Almost never perform a fluorescein angiography, *except*:

- Before focal laser is performed, as detected on OCT
- Suspected macular ischemia
- To rule out other diagnoses

What to expect from OCT in DM?

Key signs for diabetic macular edema on OCT imaging are:

- Retinal thickening
- Cystoid macular edema
- Subretinal fluid / serous retinal detachment
- Vitreomacular traction / Tractional retinal detachment



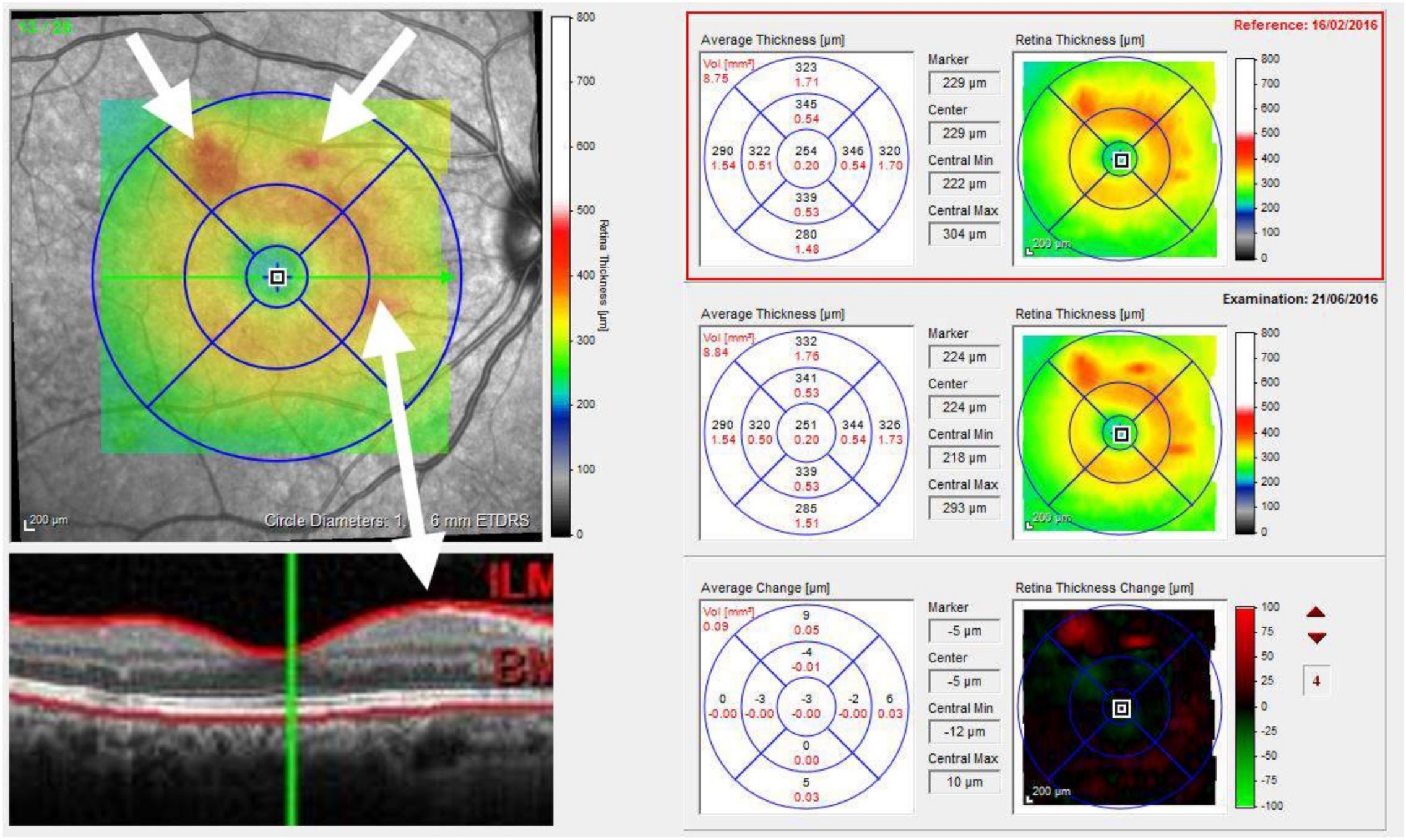
However, clearly identifying these key signs is not always that simple in practice!

With this in mind, the next section of this course will examine some example cases.

Example 1: Subclinical DME

This patient has **no retinopathy** and **normal vision**.

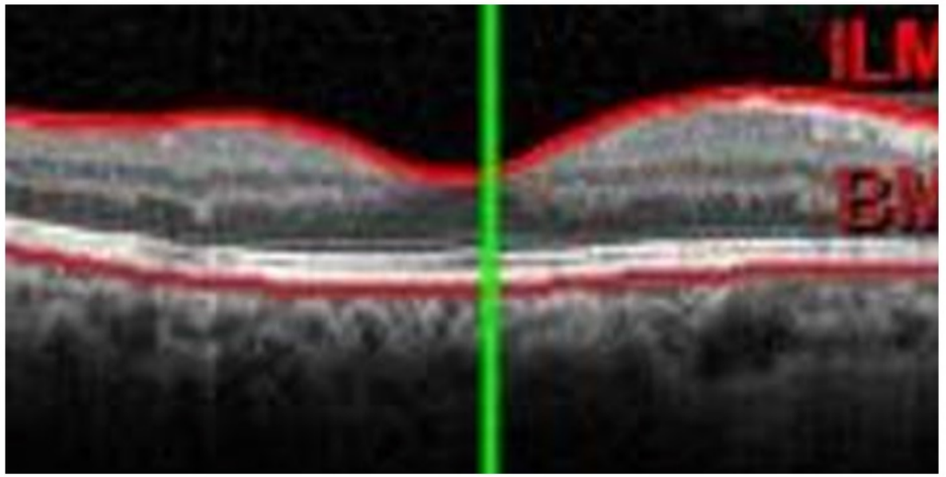
However, the macular thickness map shows a **thickening in the retina** (white arrows).



White arrows show retinal thickening on macular thickness map

Performing an OCT shows:

- No tractional retinal detachment
- No obvious retinal thickening (just a slight thickening as expected in the normal population)
- No subretinal fluid
- No cystoid macular edema



OCT imaging

This is called **subclinical DME**, and these patients develop thickening that is not easily visible.

A study by Bressler et al. (2012) had the following findings regarding **subclinical DME**:

- **High-risk to develop DME** (half of the patients will develop DME in the following 2 years)
- Beneficial **role in educating patients** (i.e. showing them pictures)
- Patients require **close follow-up**

Diabetic Retinopathy Clinical Research Network, Bressler NM, Miller KM, Beck RW, et al. Observational study of subclinical diabetic macular edema. *Eye (Lond)*. 2012; 26(6): 833-40.

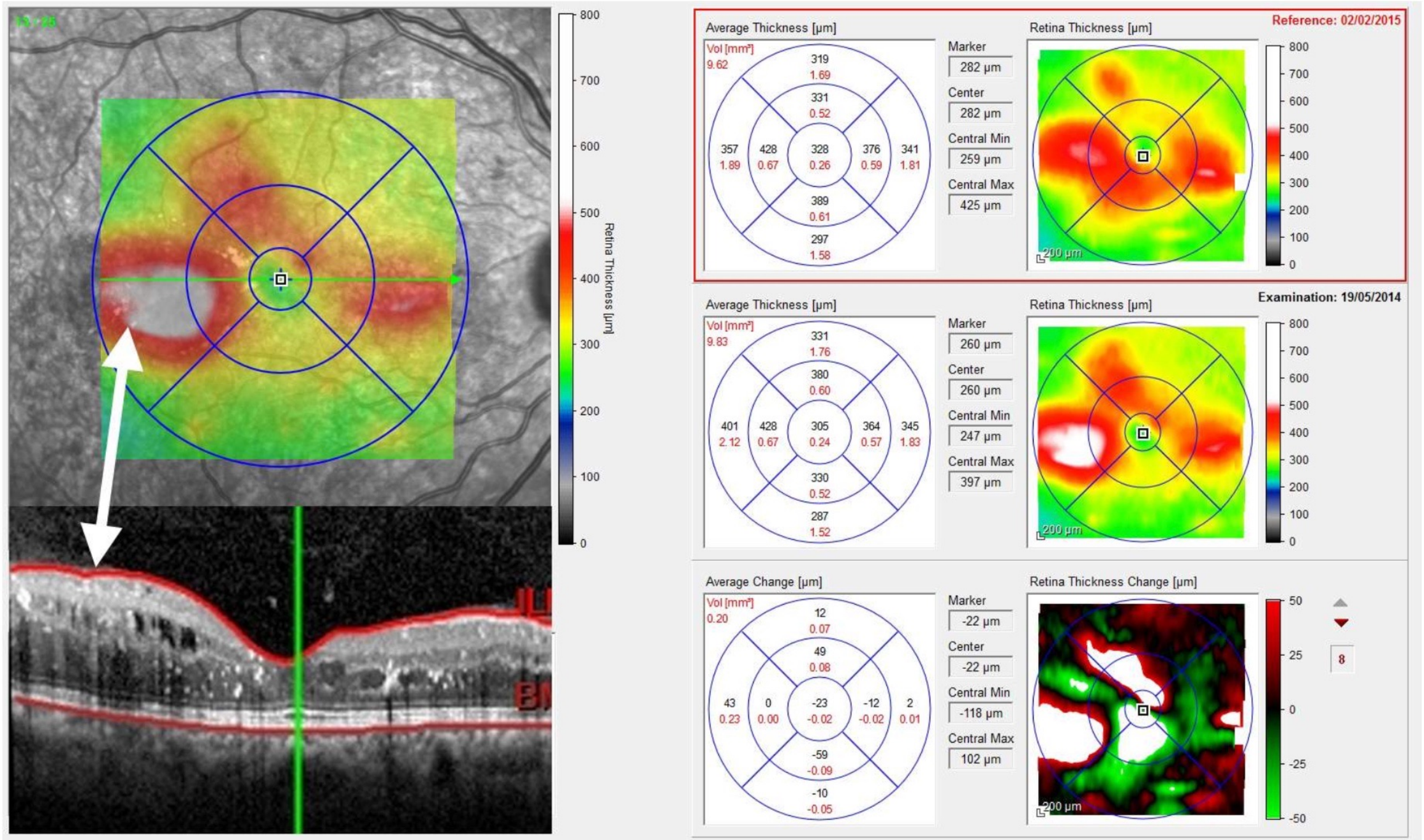
Pierre-Raphaël ROTHSCHILD (course editor) recommends to:

Always perform an OCT

Example 2: Non-centre involving DME

This patient has **non-centre involving DME**, and therefore intravitreal anti-VEGF injections are not needed.

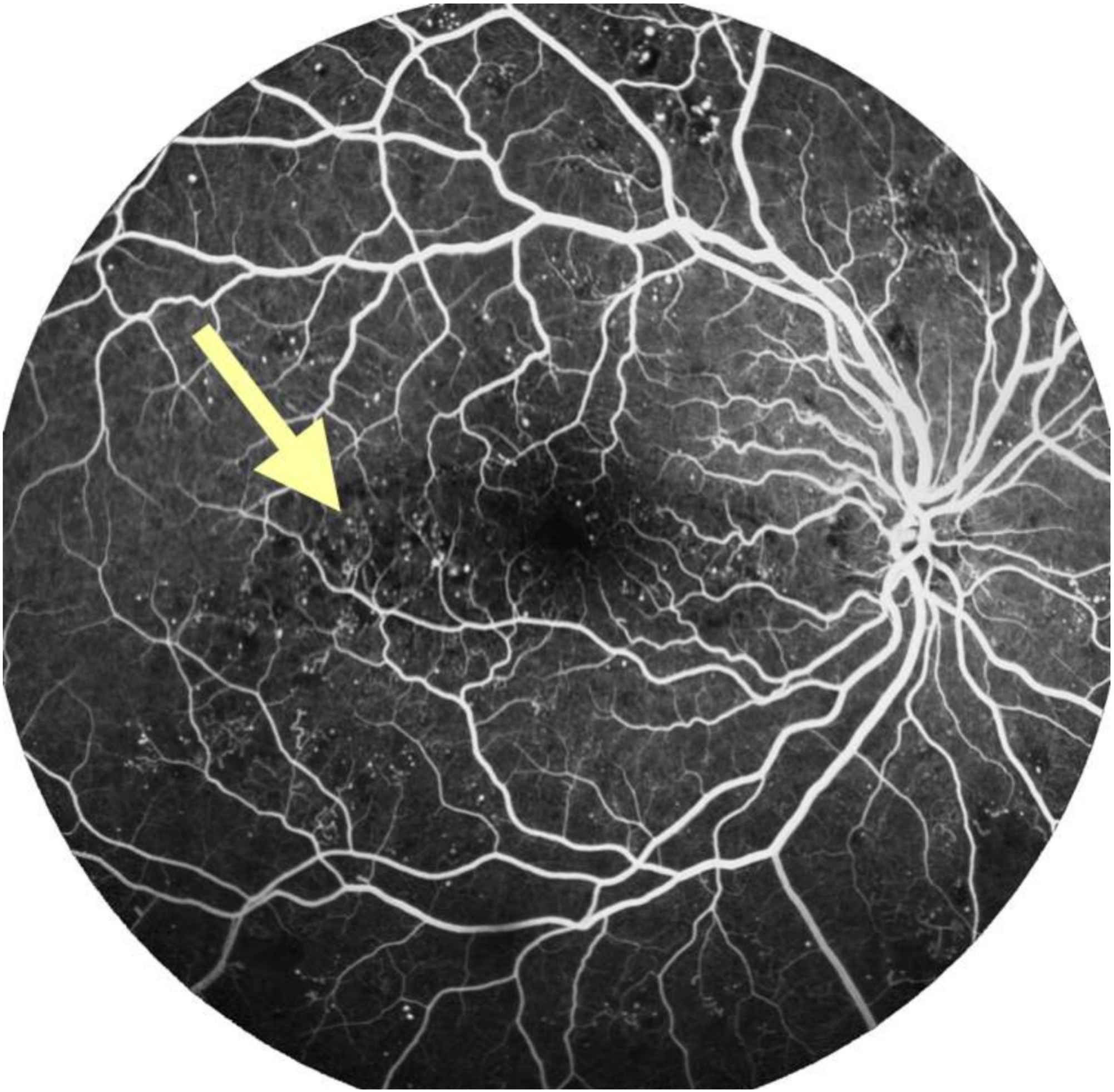
Even though this is a case of non-centre involving DME, the patient still has **moderate DME** that threatens the macula and will, therefore, require intervention.



White arrow shows non-centre involving DME (moderate DME) that threatens the macula

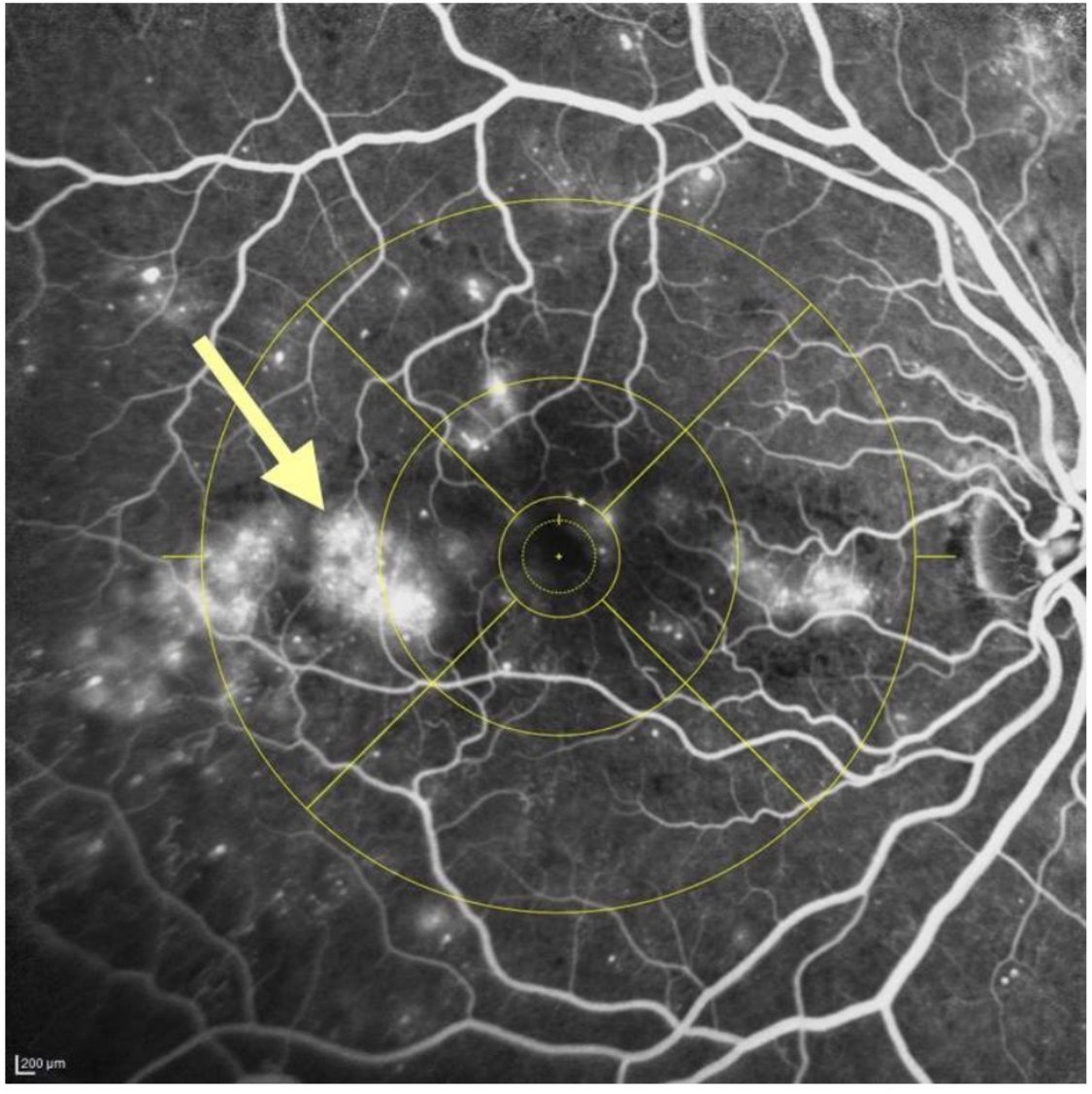
Use Early-Stage Angiography to Look for Microaneurysms

The early-stage fluorescein angiogram below shows **microaneurysms** in this patient.

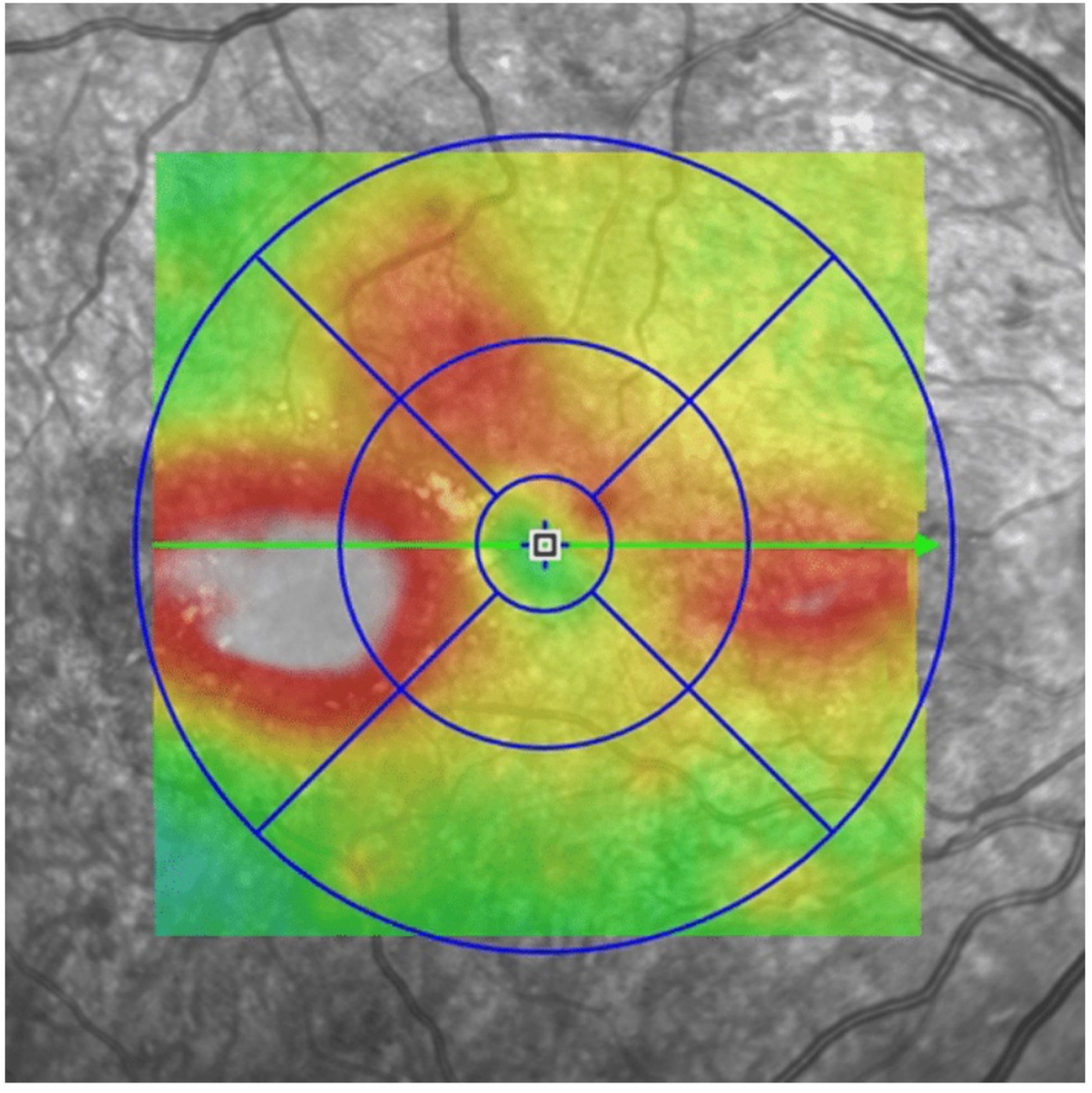


Use Late-Stage Angiography to Look for Leakage

The late-stage fluorescein angiogram below shows **leakage** in this patient.



Late-stage angiogram (arrow showing **leakage**)



OCT macular thickness map

Treatment

The patient has the **indications for laser surgery** (focal laser treatment):

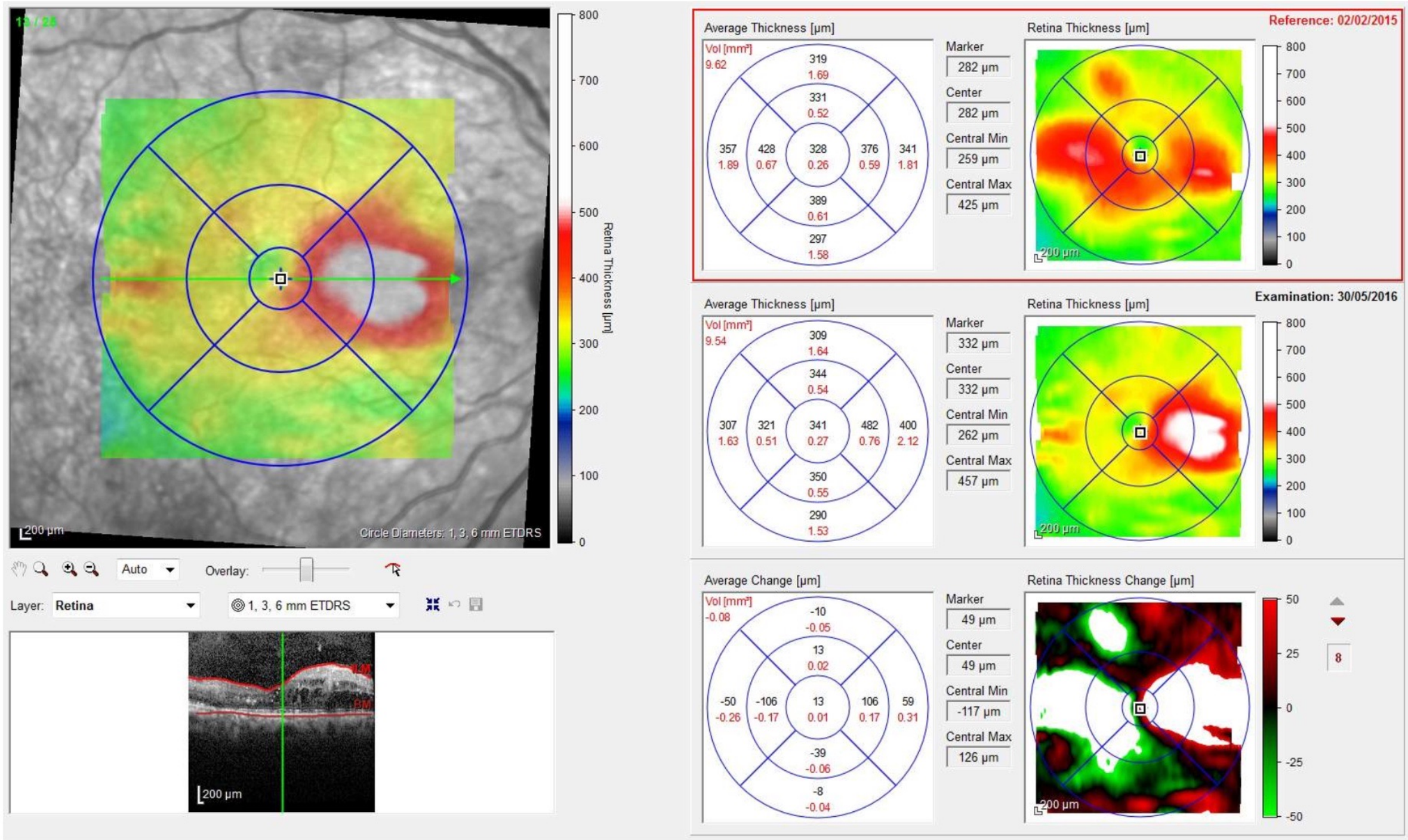
- Normal vision *and*
- Peripheral DME

Patients with these indications can really benefit from first-line laser.

Focal laser treatment was performed on this patient, and it worked quite well.

3 Months After Focal Laser Treatment

3 months later, the OCT macular thickness map shows that the patient now has **no DME on the temporal side**.



3 months after focal laser, no longer DME on the temporal side

---

Follow Up Treatment

However, the patient then required further focal laser treatment for the intrapapillary macular bundle DME (as seen on the nasal side, 3 months later).

Example 3: Use of OCT + FA

Use of FA to identify large areas of capillary nonperfusion

As examined earlier in the course, fluorescein angiography may be used in combination with OCT to help identify large areas of capillary nonperfusion.

TABLE 5 USE OF FLUORESCEIN ANGIOGRAPHY FOR DIABETIC RETINOPATHY

Situation	Usually	Occasionally	Never
To guide laser treatment of CSME	•		
To evaluate unexplained visual loss	•		
To identify suspected but clinically obscure retinal neovascularization	•		
To identify areas of vitreomacular traction		•	
To rule out other causes of macular swelling		•	
To identify large areas of capillary nonperfusion		•	
To evaluate patients with difficult and/or questionable examinations for DME		•	
To screen a patient with no or minimal diabetic retinopathy			•

CSME = clinically significant macular edema; DME = diabetic macular edema

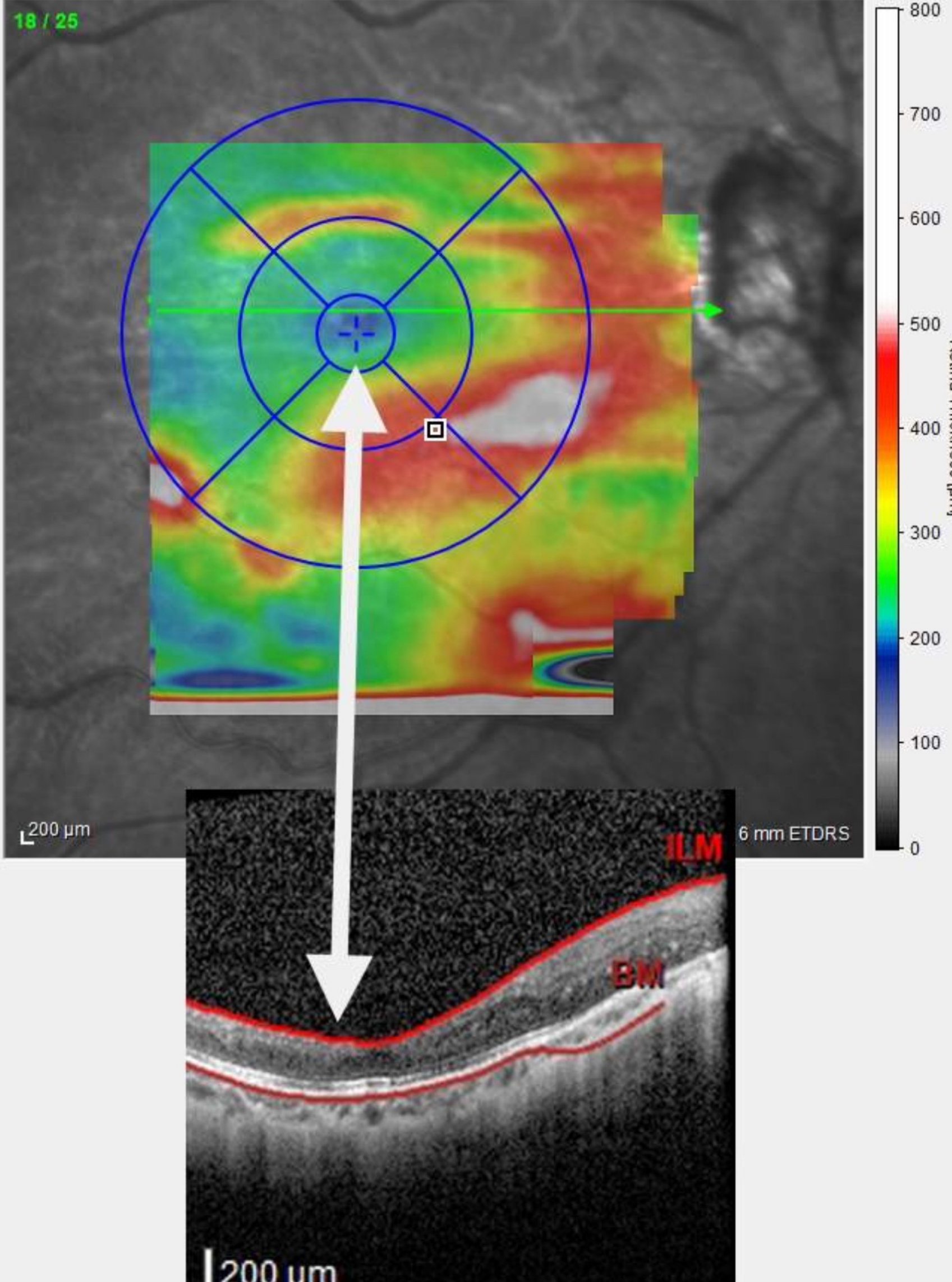
Use of FA for DR (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

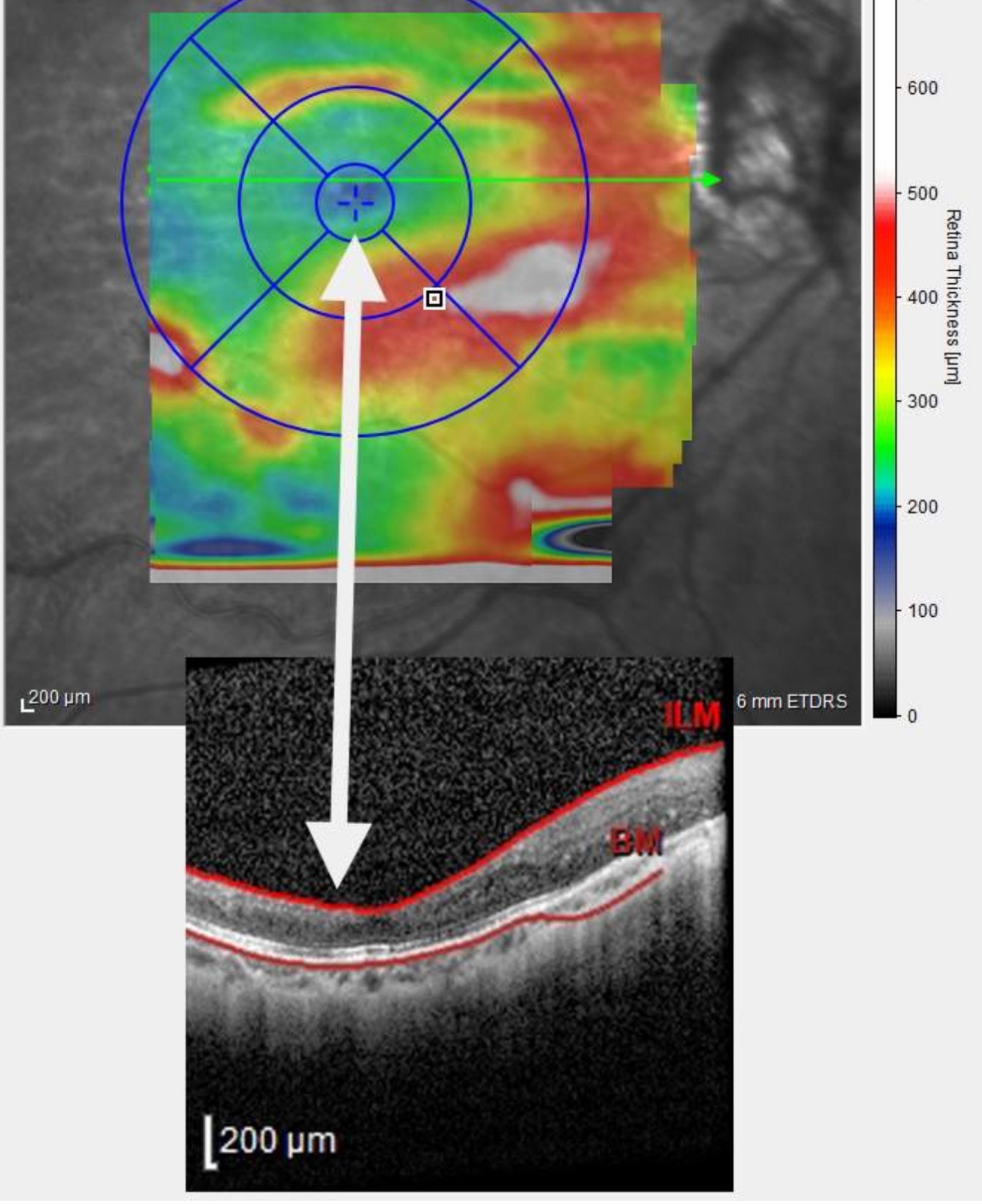
Example 3

30-year-old patient who presented with **counting-finger vision in both eyes** (OU).

The **blue area** seen on the macular thickness map (image below) indicates some atrophy on the retina.

However, the OCT looks quite normal and cannot explain this blue area nor the massive visual loss experienced by the patient.

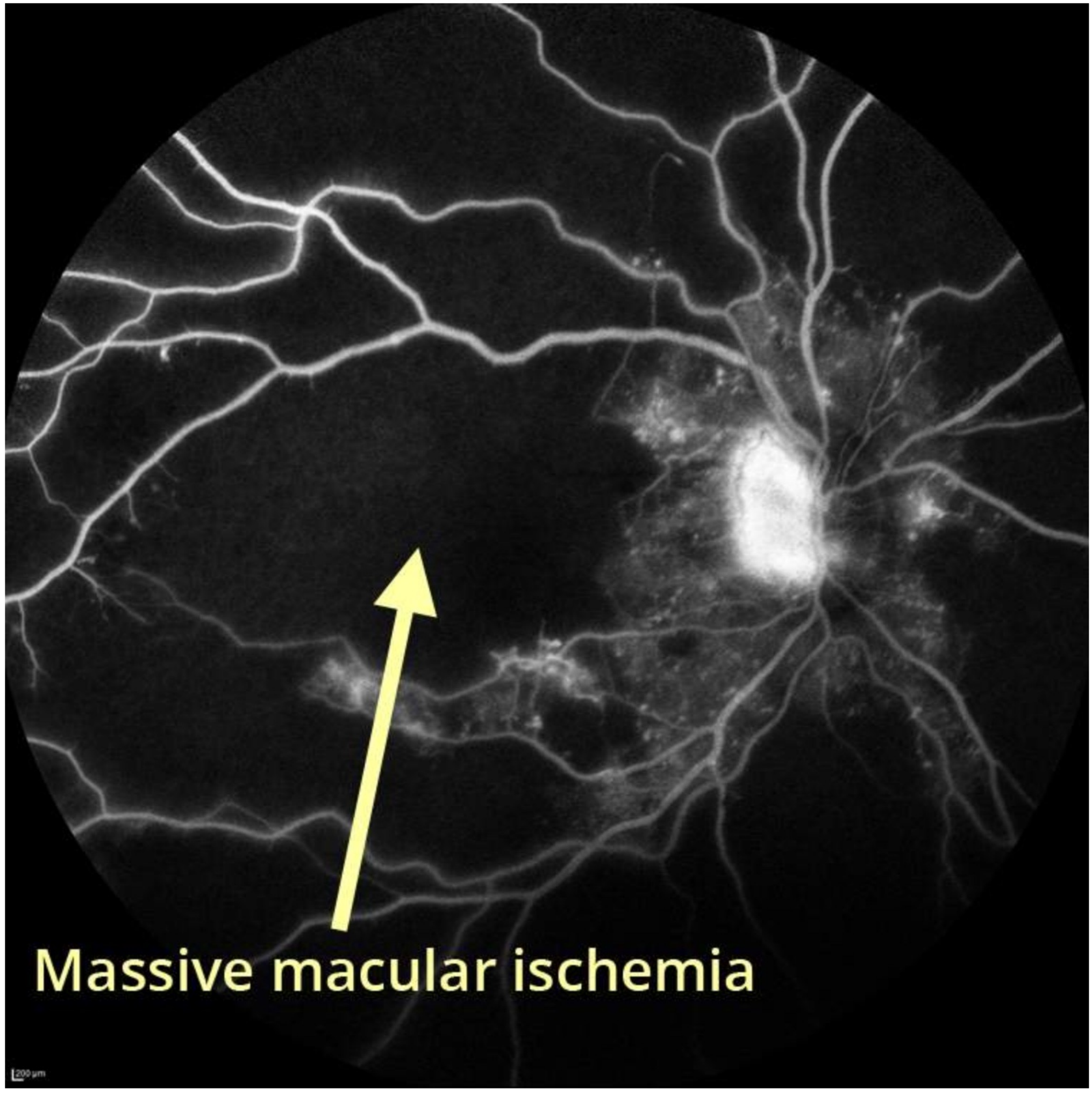

18 / 25
800
700
600
500
400
300
200
100
0
Retina Thickness [µm]
200 µm
6 mm ETDRS
ILM
BM
200 µm



Young patient (30 yo) with counting-finger vision OU

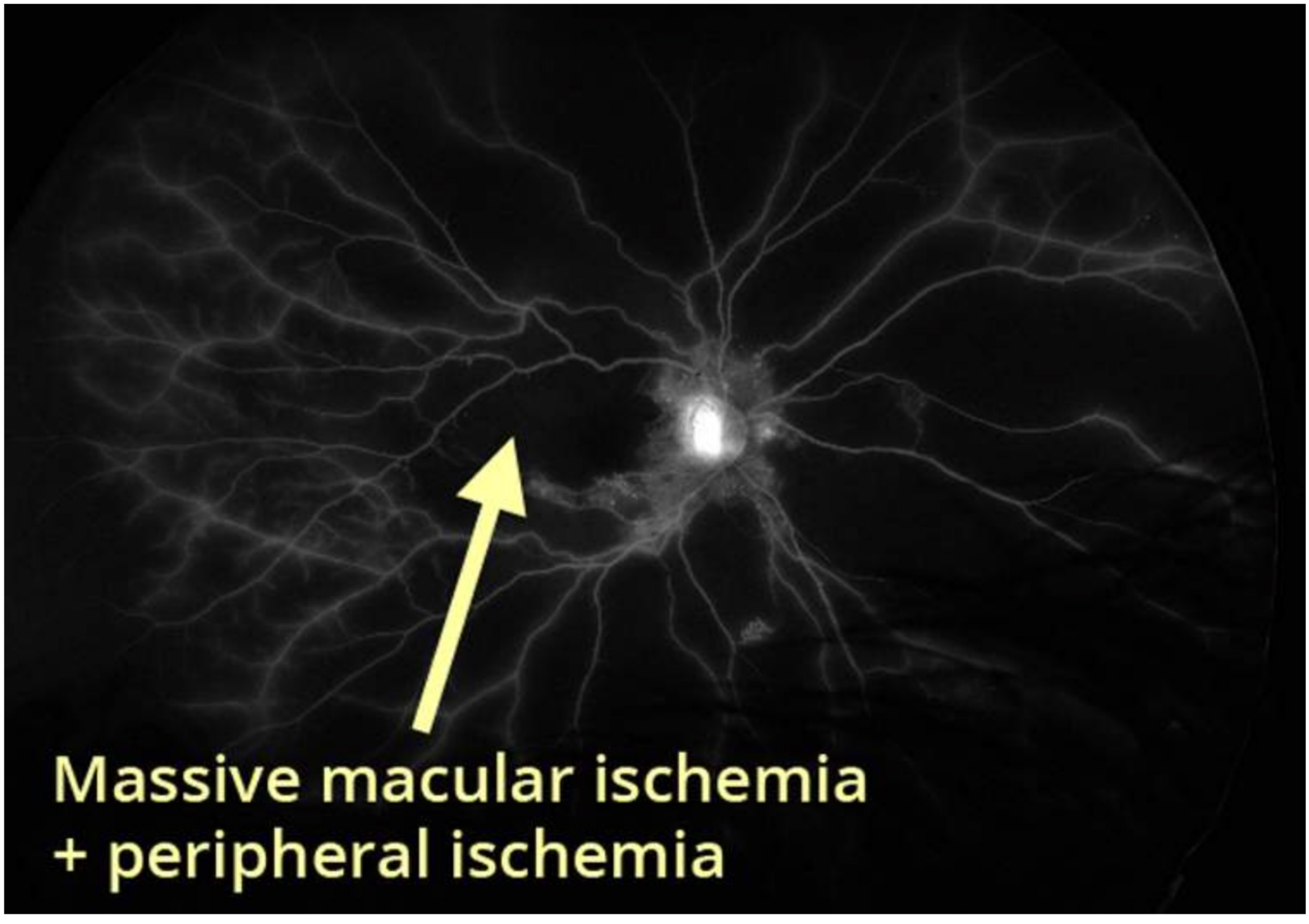
This combination of presentation and imaging findings is an indication for using fluorescein angiography.

Fluorescein angiography shows massive **macular ischemia** (capillary nonperfusion) in the patient.



FA showing massive macular ischemia

Also, in this case, fluorescein angiography shows that the patient has **peripheral ischemia**.



Fluorescein angiography shows massive macular ischemia & peripheral ischemia

The prognosis in these types of cases is very poor.

This example highlights the benefit of using fluorescein angiography in certain cases. FA reveals and explains the issue with this patient, which could not be easily explained or identified on OCT.

Example 4

Use of FA to rule out other causes of macular swelling

As examined earlier in the course, fluorescein angiography may be used in combination with OCT to help rule out other causes of macular swelling.

TABLE 5 USE OF FLUORESCEIN ANGIOGRAPHY FOR DIABETIC RETINOPATHY

Situation	Usually	Occasionally	Never
To guide laser treatment of CSME	•		
To evaluate unexplained visual loss	•		
To identify suspected but clinically obscure retinal neovascularization	•		
To identify areas of vitreomacular traction		•	
To rule out other causes of macular swelling		•	
To identify large areas of capillary nonperfusion		•	
To evaluate patients with difficult and/or questionable examinations for DME		•	
To screen a patient with no or minimal diabetic retinopathy			•

CSME = clinically significant macular edema; DME = diabetic macular edema

Use of FA for DR (Table from AAO, Diabetic Retinopathy Preferred Practice Patterns - Update 2017)

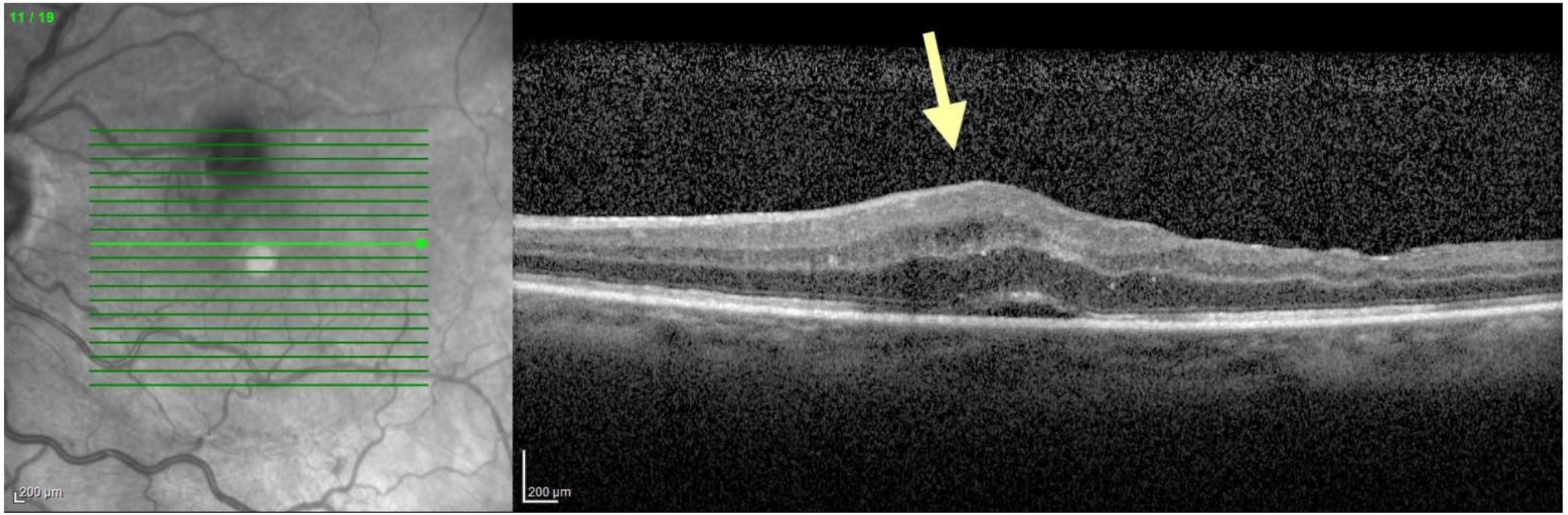
However, **FA is not always needed to rule out other causes**, as in the case below.

Example 4

This is a 58-year-old patient with **longstanding uncontrolled diabetes** and **visual loss**.

OCT imaging shows:

- Retinal thickening
- Cystoid macular edema
- Subretinal fluid / serous retinal detachment



OCT shows retinal thickening, CME and SRF/SRD

These are all the conditions to diagnose diabetic macular edema.

However, a lesion is seen in the upper part of the macula on the fundus projection.

Lesion seen in upper part of the macula on the fundus projection

Performing a B-scan through this lesion shows a **macular aneurysm** - this then explains the macular edema.

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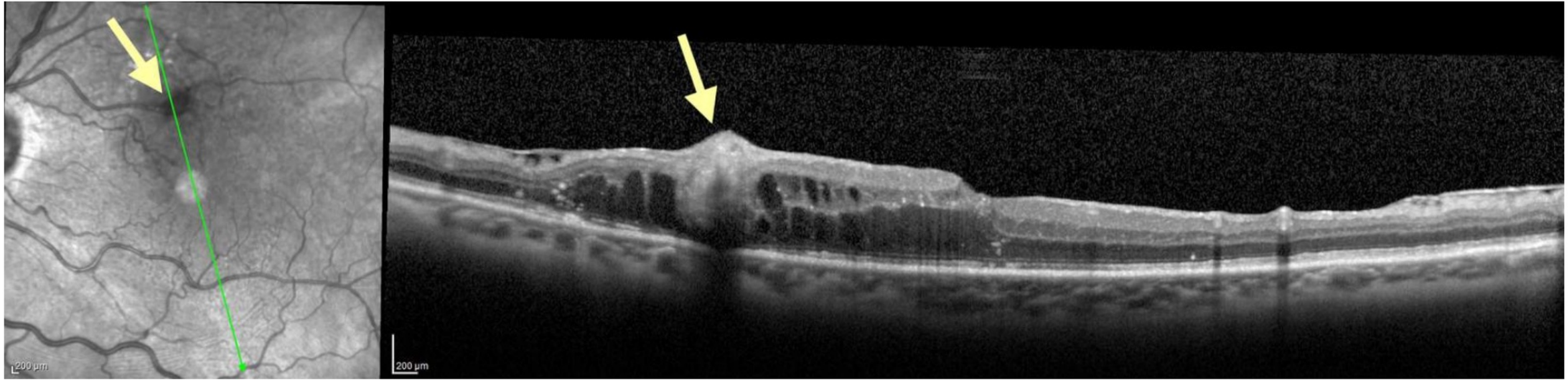
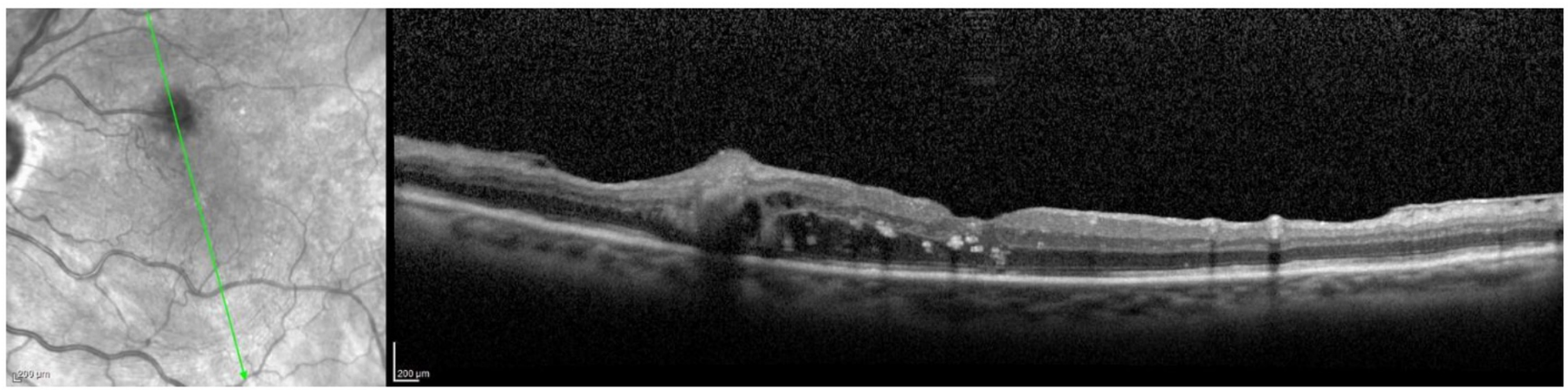


B-scan through lesion shows a macular aneurysm

Treatment

The patient is treated with focal laser treatment only (and not treated with anti-VEGF injections).

TREATED WITH FOCAL LASER	3 MONTHS AFTER FOCAL LASER	6 MONTHS AFTER FOCAL LASER



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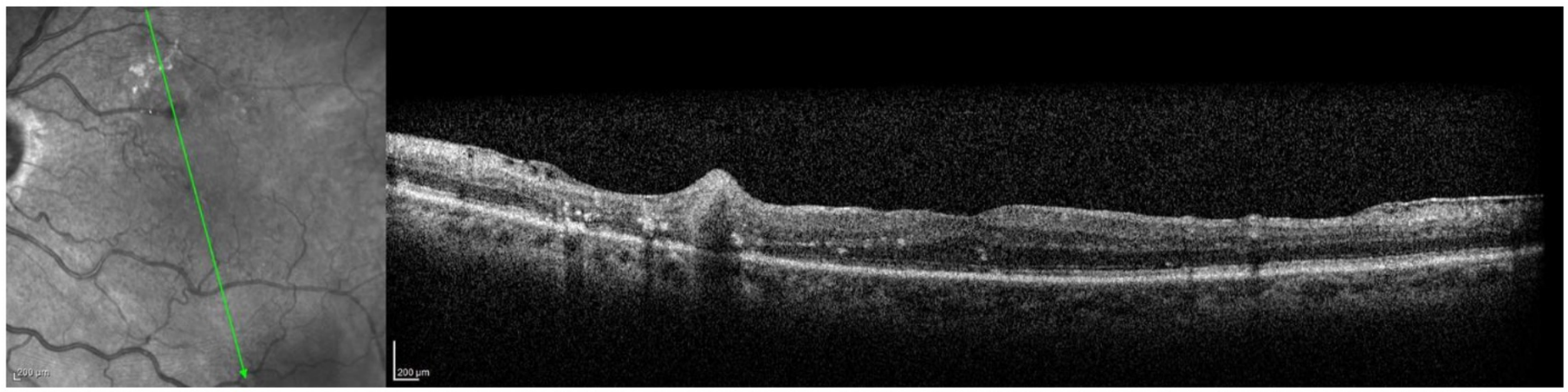

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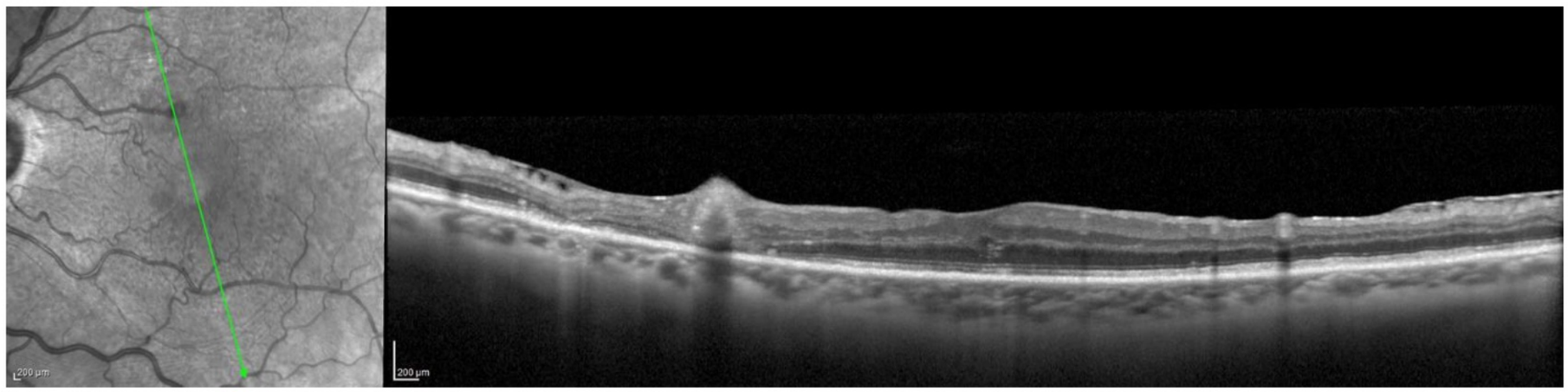


So, with close examination using OCT (and not always requiring fluorescein angiography) other causes can be ruled out, and then these patients do not have the burden of anti-VEGF injections.

Example 5: TRD

Tractional retinal detachment

The final situation regarding what to expect from OCT in DM is in relation to "**Vitreomacular traction / Tractional retinal detachment**".

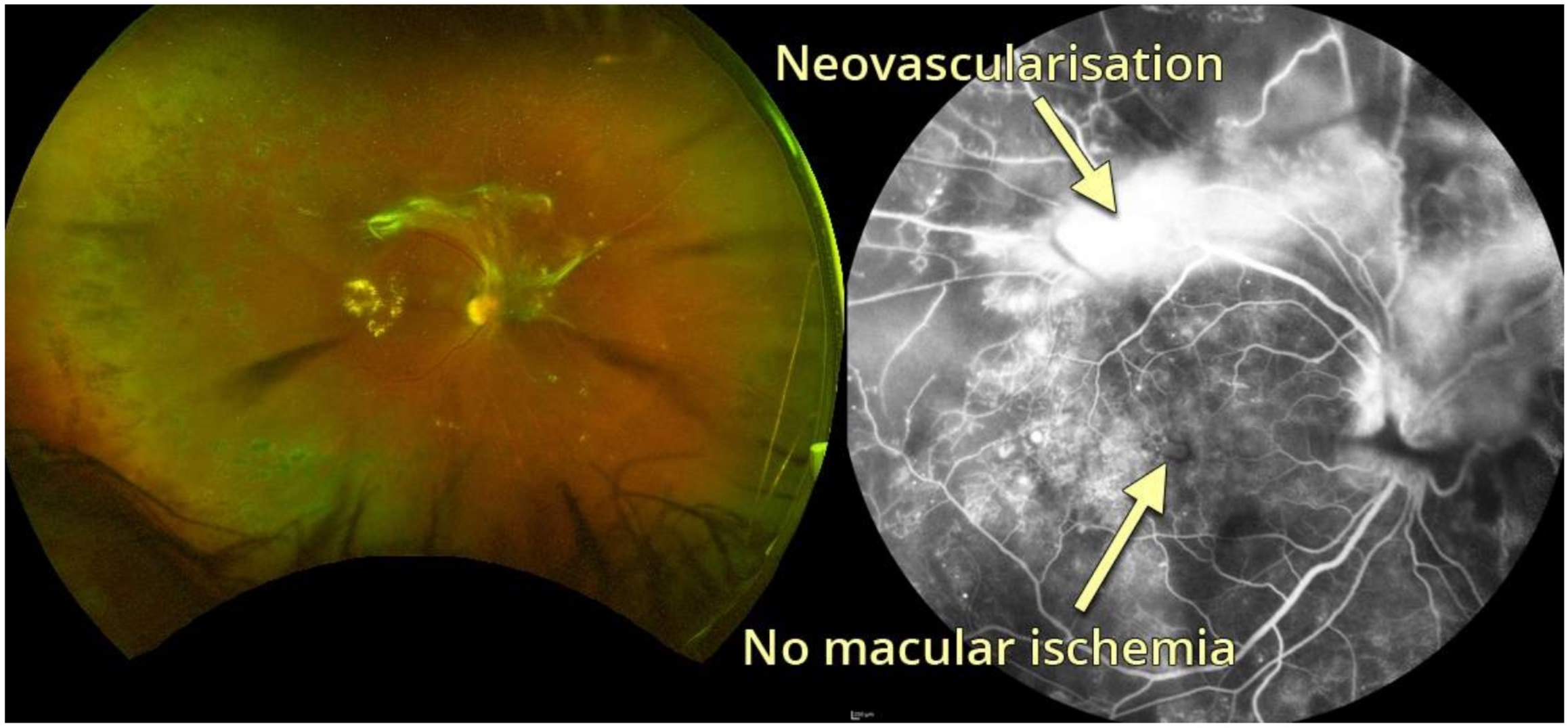
Example 5

40-year-old female patient with obviously **severe DME in both eyes**.

Colour fundus photography shows **exudates in the fovea** and also **proliferative diabetic retinopathy**.

Colour fundus photography showing exudates in the fovea and proliferative diabetic retinopathy

An angiogram shows very severe **neovascularisation**. However, it also shows that this patient has **no macular ischemia** - so, potentially a good prognosis after surgery.

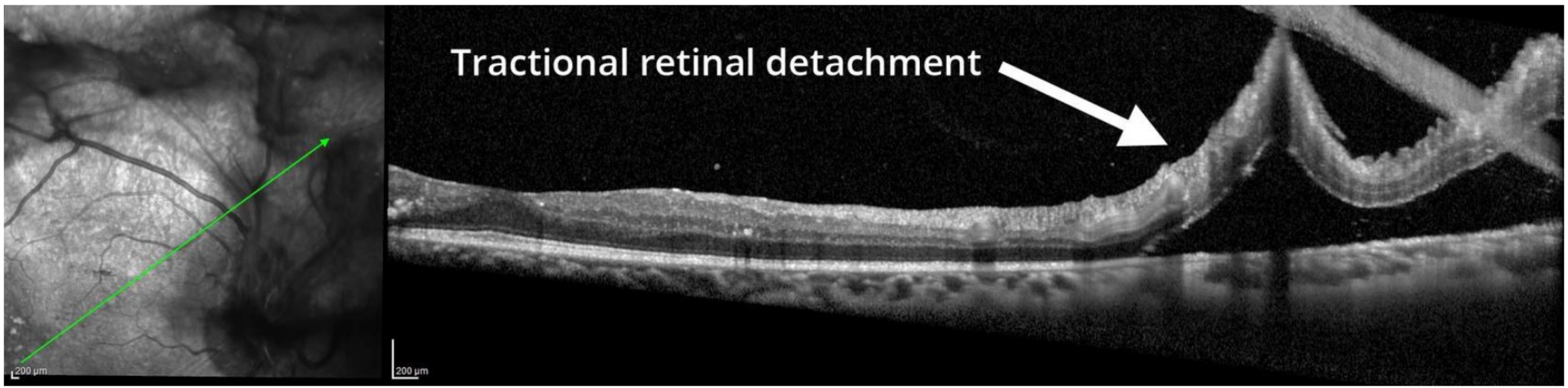


Angiogram shows neovascularisation but no macular ischemia

Follow-up:

Unfortunately, this patient was lost to follow-up.

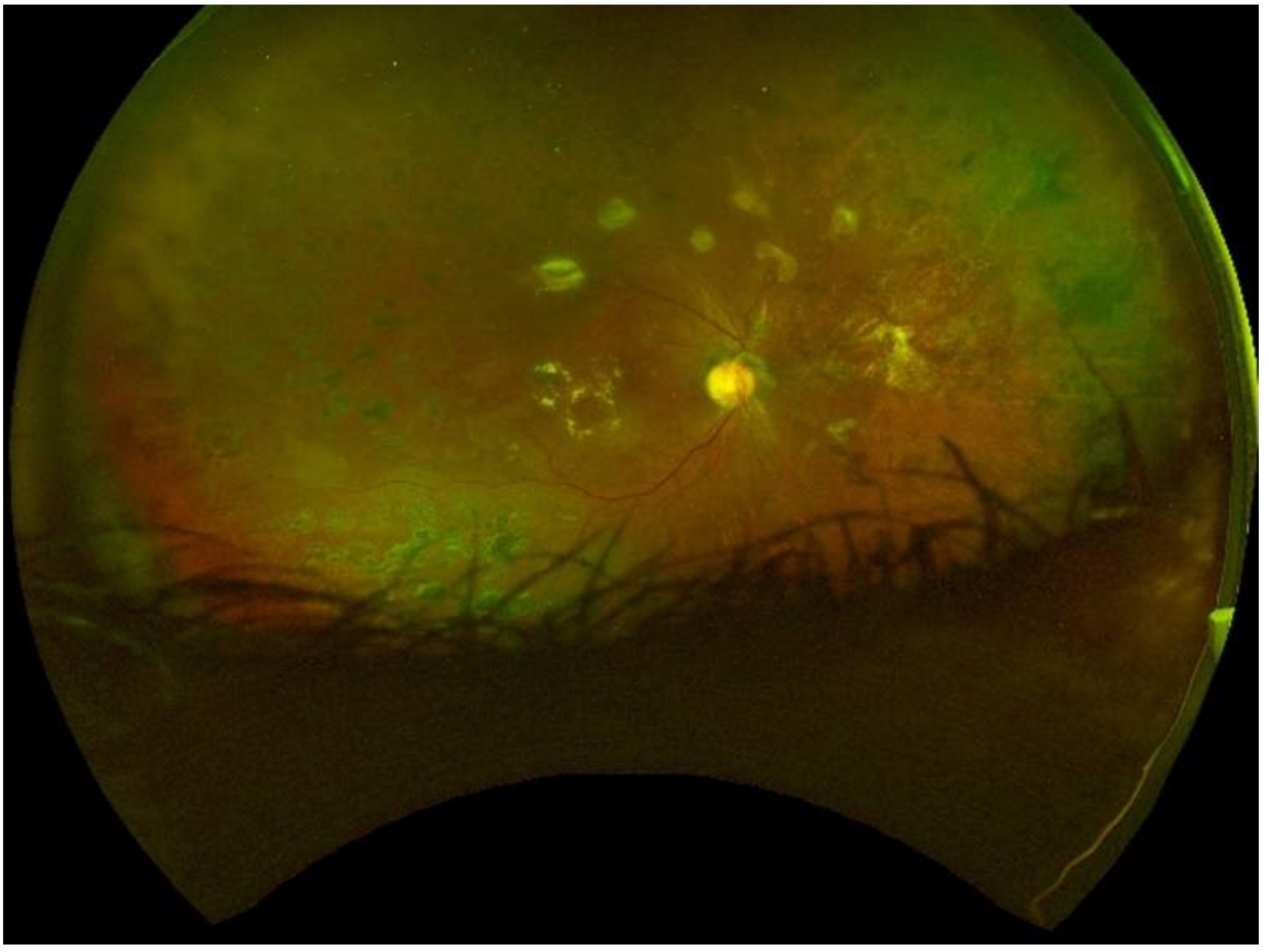
She came back a couple of months later with **macula-off tractional retinal detachment**.



OCT showing tractional retinal detachment

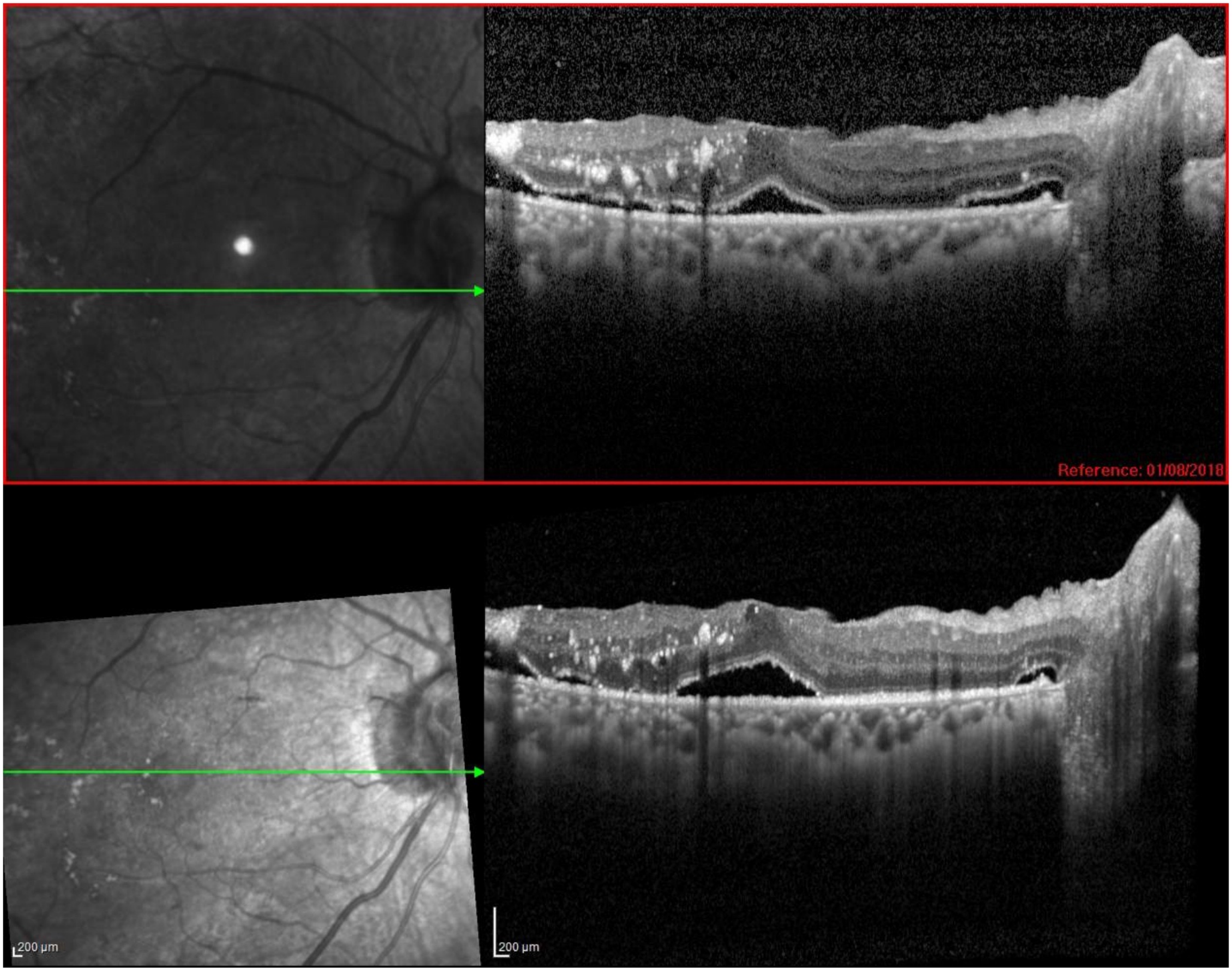
Post-Surgery:

Surgery was performed and she improved to almost normal vision.



Post-surgery colour fundus photograph

Note that subretinal fluid may still be seen in these cases post-surgery, as a chronic serous detachment can take several weeks, or even months, to clear.



This patient improved over time and has almost normal vision now.

Summary

Key messages from this course:

- Always perform OCT for patients with diabetes mellitus
- Use fluorescein angiography when necessary
- Tailor treatment according to OCT ± Angiography to choose between:
  - IVT
  - Laser
  - Surgery