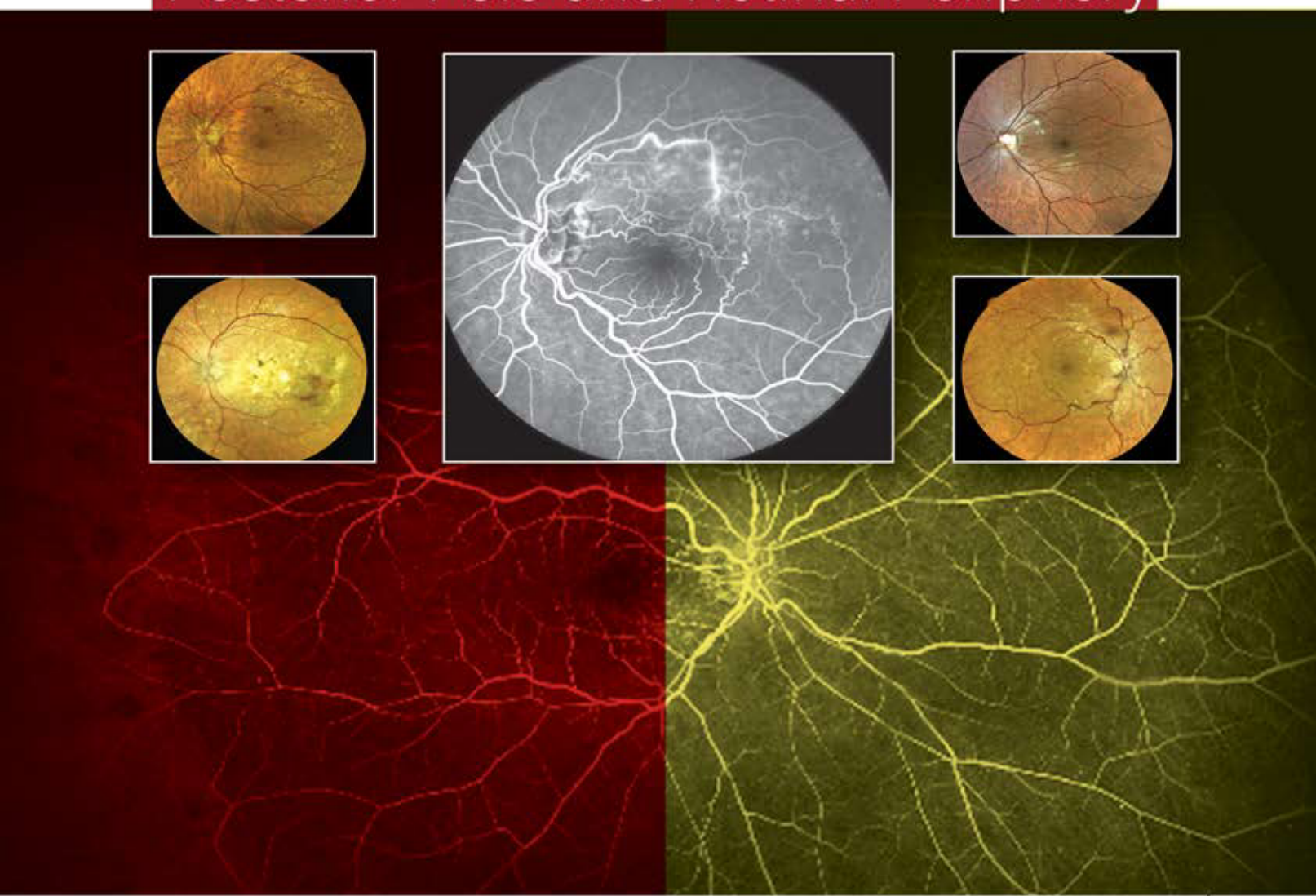
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# Practical Handbook of Fluorescein Angiography

## Posterior Pole and Retinal Periphery



Marco Rispoli
Bruno Lumbroso

2nd Edition

JAYPEE

# Practical Handbook of FLUORESCEIN ANGIOGRAPHY

## Posterior Pole and Retinal Periphery

## SECOND EDITION

### REVISED AND ENLARGED


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# Contents


Preface to the second edition v
Preface to the first edition vii
Dedication ix
Acknowledgments ix
Contributors xiii

**PART I: INTERPRETING A NORMAL AND PATHOLOGICAL FLUORESCEIN ANGIOGRAPHY**

**Chapter 1**
Retinal anatomy and fluorescein angiography 1

**Chapter 2**
Normal fluorescein angiography of the central retina 5

**Chapter 3**
Normal fluorescein angiogram of the optic disk 9

**Chapter 4**
Normal fluorescein angiography of the choroid 11

**Chapter 5**
Interpreting a pathological fluorescein angiography 13

**PART II: NEW DYELESS IMAGING FOR RETINA AND CHOROID STUDY: OCT AND OCT-ANGIOGRAPHY**

**Chapter 6**
Assessment of fluorescein and indocyanine angiography versus OCT-angiography: Fluorescein angiography/OCT-angiography: A progressive transition 17

**PART III: PATHOLOGICAL FLUORESCEIN ANGIOGRAPHY ANALYTICAL STUDY**

**Chapter 7**
Abnormal hyperfluorescence 25

**Chapter 8**
Abnormal hypofluorescence 49

**Chapter 9**
Abnormalities in circulation time 57


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## PART IV: PATHOLOGICAL FLUORESCEIN ANGIOGRAPHY-SYNTHESIS

**Chapter 10**
Synthetic evaluation 59

## PART V: MAJOR FLUORESCEIN ANGIOGRAPHY SYNDROMES POSTERIOR POLE

**Chapter 11**
Diabetic retinopathy 63

**Chapter 12**
Age-related macular degeneration and other macular degenerations 75

**Chapter 13**
Vascular occlusions 89

**Chapter 14**
Pachychoroid spectrum of disorders: Retinal epitheliopathies 97

**Chapter 15**
Vitreoretinal interface syndrome 103

**Chapter 16**
Diagnosis of a dark area in the fluorescein angiography 105

**Chapter 17**
Inflammatory disorders 109

## PART VI: FLUORESCEIN ANGIOGRAPHY STUDY OF RETINAL PERIPHERY

**Chapter 18**
Fluorescein angiography of the retinal periphery 113

**Chapter 19**
Retinal periphery in diabetic retinopathy 123

**Chapter 20**
Widefield angiography in ocular oncology 131

## PART VII: CONCLUSION

**Chapter 21**
The future of fluorescein angiography 141

**Index** **145**


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# Chapter 6

# Assessment of fluorescein and indocyanine angiography versus OCT-angiography

## Fluorescein angiography/OCT-angiography: A progressive transition

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## INTRODUCTION

Until 2014 the only possibility for vascular evaluation was dye angiography, using fluorescein or indocyanine green (ICG) angiography. Since that date, a new technology, optical coherence tomography-angiography (OCT-A), has rapidly developed and substituted in many cases of the invasive dye angiography. The method is easy, fast, and innocuous, it gives no side effects, and can be repeated many times without problems for the patients. OCT-A imaging is at present largely used in retina practices. It gives, in the study of many disorders, faster and more precise results than fluorescein angiography (FA). This is easily seen for choroidal neovascularization (NV). Neovascular cells leak fluid. FA utilizes this characteristic to identify neovascular tissue. Dye leaking from vessels is visualized during angiography. The main shortcoming of dye imaging is that it identifies exudation from NV and not NV itself. It is an indirect diagnosis that can cause errors. OCT-A exudative vessels and also nonexudative new vessels that are not seen on FA. OCT-A shows blood flow and structural information that is not possible to see with dye-based imaging. It offers good visualization of the neovascular network, choriocapillaris, and choroid compared with dye angiography. OCT-A does not depend on vessel wall leakage, it allows a better diagnosis of NV, detecting directly both nonexudative and exudative NV and giving a better understanding of other retinal abnormalities physiopathology. Structural OCT can identify exudation from these vessels. Let us say right away that, any old fluorangiography specialist was at first disconcerted when he saw the first angiography OCT imaging. There were new bearings. Lack of leakage, of staining, and of pooling makes angiography OCT images too sharp, too "dry". Vascular circulation with angiography-OCT looks different from FA.

A limiting factor is that many retina physicians are not yet perfectly trained to OCT-A imaging interpretation.

Until a few years ago, FA *was the clinical gold standard* for diagnosis, monitoring evolution, and deciding when and how to treat. It is now being progressively replaced by OCT-A. OCT-A in everyday practice is increasingly substituting FA and indocyanine angiography. As a matter of fact, OCT-A allows clinicians to view simultaneously both the tissue structure and the blood flow in retina and choroid. We are witnessing a pivotal transition taking place in clinical everyday imaging.

Optical coherence tomography-angiography and fluorescein angiography yield quite different data. Comparing the characteristics of the two methods is not an easy or a simple process. We have to apply a logical method to interpret the different data the two angiography methods produce.

We cannot study the OCT-A scans as we study FA and ICG imaging.

In fluorangiography all the retinal layers are merged. FA provides *two-dimensional* (2D) pictures; in FA the vessels appear to be overlaid and superimposed in one layer. OCT-A allows to study separately the different retinal and choroidal layers.

Fluorangiography is a *dynamic* imaging process that is partly obscured by dye leakage and staining. It is a dynamic examination, with a stated duration in time. It has a beginning and an end, with initial, intermediate, and late frames.

Fluorangiography does not allow to measure or quantify blood flow, flow speed, capillary density, and capillary loss. Fluorangiography highlights vessel walls damages that are not clinically visible. Vessel wall leakage and wall staining are functional lesions not yet visible on OCT-A. It identifies leakage from NV and not NV itself. Nonexudative new vessels that are not seen on FA. OCT-A shows *static* images, but they are more precise and details are sharper.

## ADVANTAGES AND DISADVANTAGES OF FLUORESCEIN ANGIOGRAPHY

Fluorescein angiography is an invasive procedure, with medicolegal problems, insurance is necessary. Injecting dye may cause side effects. There is a learning curve. FA procedure is more expensive than OCT-A. There are costs: nurse, dye, and injection. In many countries, as in Italy we need the attendance of an anesthetist-reanimator present, there are costs of insurance for invasive procedure. FA gives no quantitative data. Practically, it needs appointment not always immediately available in office or hospital. It is anyway still useful in retinal periphery and inflammations.

Fluorescein angiography shows the dye leakage, its pooling in the intraretinal and subretinal cavities, and the staining of the vascular walls. It allows to explore retinal periphery.

### Invasive procedure side effects

Fluorescein angiography is invasive and causes discomfort for the patient, such as nausea, vomit, syncope, and severe (but rare) complications such as general allergic reactions and quincke's edema. Severe cardiac and cardiovascular complications are rare but there

have been cases of anaphylactic shock. Death during procedure is exceptional; however, this possibility is an obvious worry if the patient suffers from severe general problems.

Fluorescein angiography is not advised in elderly people, in heart patients, and in pregnant women. In addition, FA produces also a higher number of nongradable images. Repeating an invasive examination is not well-accepted.

Optical coherence tomography-angiography: OCT-A is a noninvasive three-dimensional (3D) examination.

It is motion contrast-based: Flow is extracted from serial consecutive images.

It is a static examination; there are no differences between the images at a given moment and the images captured an hour or a day later. Even though OCT-A is based on blood movement, the structure, the retina, is static.

Optical coherence tomography-angiography imaging gives a cast of blood circulation, vessels branching, and dividing till the smallest capillaries, anastomoses, shunts, and capillary dropout. It gives us, with more precision vessel intravascular shape.

We are able to measure exactly and quantify blood flow, capillary density, capillary loss, and other quantifiable elements. We obtain different data from those attained by dye angiography.

## ADVANTAGES AND DISADVANTAGES OF OCT-ANGIOGRAPHY

Optical coherence tomography-angiography is a very efficient procedure, that saves doctors and patient time: OCT-A lasts 3 minutes, while complete FA with recording of late phases lasts 20 minutes. Patients accept easily a noninvasive procedure. It is absolutely safe and safety is a long-term investment. Safe repeatability is a great advantage.

Subsequent costs are slight.

Technology allows fast clinical decision, better clinical flow, and better efficiency.

One of the most important clinical advantages is that it gives quantitative data that FA does not give, and that it gives more qualitative data than FA. It shows separately retinal layers and vascular networks. OCT-A will not be used the same way as FA.

*Interpretation methodology is quite different. OCT-A will not be used the same way as FA. Operator should learn a new and quite different method, and the learning curve is generally short. It may be sometimes tricky. You cannot use your FA knowledge for OCT-A interpretation*:

Artifacts were a big problem with the first OCT-A devices. These difficulties are now greatly reduced. With FA you do not see the flow itself, you see the dye that leaks, pools, stains, and you only deduce the blood flow. With OCT-A you see directly the blood flow itself, and structural OCT shows you the hard structures, wall, etc.

Practically, in many countries OCT-A scans are not reimbursable. The device has a high initial cost, but everyday expenses are lower than FA.

Optical coherence tomography-angiography gives (less expensive, safer, more comfortable for patient and operator, easier, and faster) most of the information that FA does. Information not given can easily be bypassed. It is not used the same way as FA.

We insist on the fact that it is a noninvasive method. This non-invasive test offers tranquillity to both patient and ophthalmologist. It is possible to repeat it frequently, if needed, and the patient can be easily monitored. It can be repeated even in elderly people, in heart patients, and in pregnant women. OCT-A modern devices allow the retinal periphery examination. The main advantage of OCT-A interpretation is that it is not hampered by dye leakage or it is pooling in the intra- and subretinal cavities, and there is no staining of the vessel walls. Indeed, OCT-A shows a neat and clear image of the morphology of the vessels of a given layer without the influence of staining, pooling, and leakage, and window effect that in FA, tend to quickly hide the morphology of the vessels in pathologic cases. OCT-A makes it possible to evaluate the fine vascular morphology.

There is no need to plan examination in advance. Any patient needing an angiography could and should get immediately an OCT-A.

Angio OCT implies economy in safety, insurance, time, nurse, anesthetist, electrocardiogram (ECG) and blood tests, clinical material, and syringes.

## DIFFERENCES BETWEEN FLUORESCEIN ANGIOGRAPHY AND OCT-ANGIOGRAPHY INTERPRETATION

When they first begin to use the new technology, operators should realize that OCT-A is unquestionably not a dye angiography. We cannot make a straight comparison between the images obtained from different techniques, but rather make a comparison between the known elementary lesions (known through traditional or en face B-scan analyses) (**Box 1**).

### Microaneurysms (Figures 1 and 2)

*Microaneurysm in FA*: Hyperfluorescence is due to dye accumulation, staining, and leakage. FA gives 2D location and functional importance of the lesion (the greater the leakage, the greater the wall lesion). FA does not inform on location in depth.

*Optical coherence tomography-angiography*: This is a 3D examination. The microaneurysm is not always apparent. In order to be seen and studied, the lesion must be perfused and have a detectable flow. Flow should not be too fast or too slow. The segmentation slab thickness should be equal to or greater than the size of the aneurysm. If not, the lesion will not be seen.

It is manifest that a direct comparison between FA and OCT-A is not useful.

**Box 1: Features better seen with optical coherence tomography-angiography than with fluorescein angiography**

Choroidal neovascularization (exudative and nonexudative):

- Retinal neovascularization
- Superficial retinal capillaries
- Deep retinal capillaries
- Vertical anastomoses
- Perifoveal arcades
- Lack of leakage shows better capillary abnormalities, new formed vessels
- Lack of staining shows better abnormalities of vascular network

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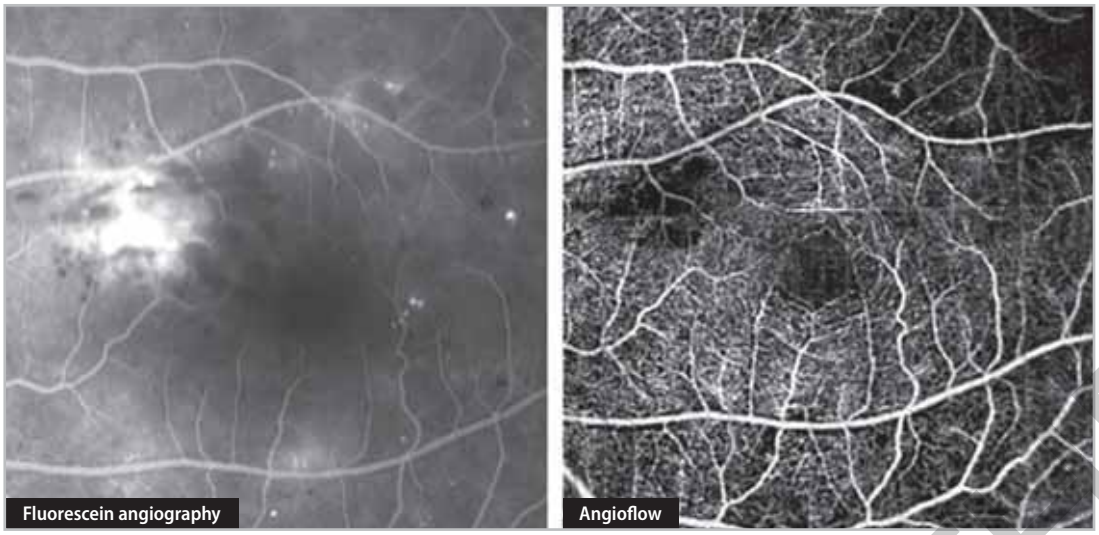



**Figure 1** Background diabetic retinopathy. Fluorescein angiography (left hand figure) and OCT-A (right hand figure). Fluorescein angiography shows dye leakage staining and pooling (microaneurysms) around some retinal vascular abnormalities. Nonperfusion areas, dye leakage, and microaneurysms are highlighted. Dye leakage prevents precise visualization of posterior pole abnormalities. In the same eye OCT-A shows more precisely and sharply areas of nonperfusion, enlargement of the avascular foveal zone with large breaks of the vascular arcade. OCT-A highlights a smaller number of microaneurysms.
(OCT-A: optical coherence tomography-angiography)

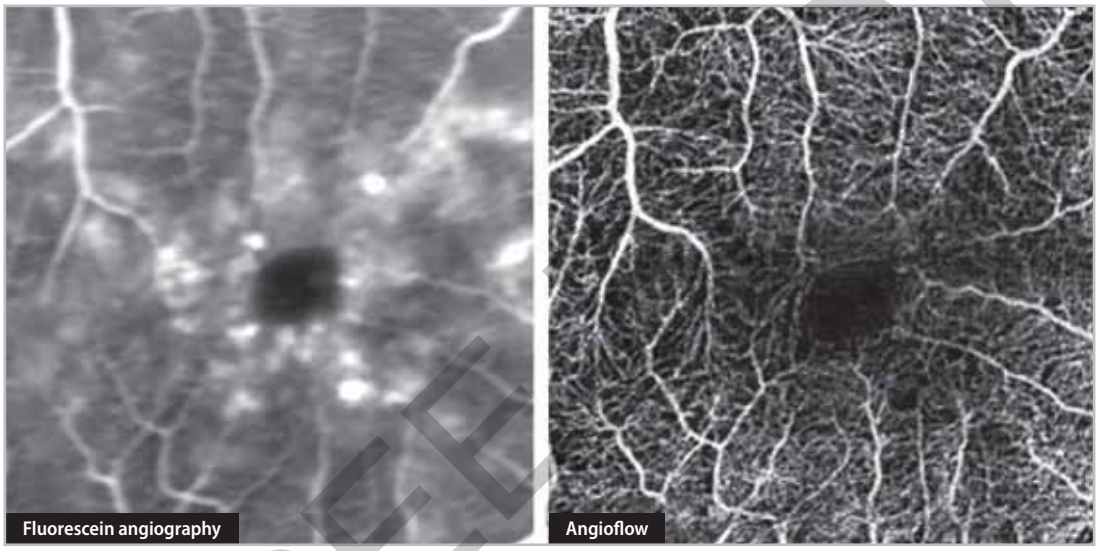



**Figure 2** Nonproliferative diabetic retinopathy. Fluorescein angiography (left hand figure) and OCT-A (right hand figure). Fluorescein angiography shows dye leakage around some retinal vascular abnormalities. Nonperfusion areas and numerous microaneurysms are hyperfluorescent. Dye leakage prevents precise visualization of vascular abnormalities. Optical coherence tomography-angiography (OCT-A) covers a smaller field but give a higher magnification. In the same posterior pole OCT-A shows areas of nonperfusion, enlargement of the avascular foveal zone with large breaks of the vascular arcade. OCT-A highlights a smaller number of microaneurysms. It does not show microaneurysms where blood flow is not fast.
(OCT-A: optical coherence tomography-angiography)

## Nonperfused areas of capillary Dropout

*Optical coherence tomography-angiography is at present used every day in most varieties of macular disease*: Vascular retinal diseases, and new vessels in age-related macular degeneration (AMD), and other disorders. It allows a sharper assessment of the posterior pole vasculature, and of macular network than FA, highlighting foveal avascular zone (FAZ) disruption and capillary dropout, without the need of an intravenous injection of fluorescein. OCT-A is a noninvasive and more sensitive procedure for detailed morphological evaluation of central macular vascular changes.

*In FA*, the two vascular plexuses are superimposed on each other and they cannot be examined separately. It highlights almost exclusively the superficial plexus and does not allow to evaluate the deep plexus. FA cannot evaluate quantitatively capillary dropout and vascular density.

*Optical coherence tomography-angiography* highlights the superficial and deep plexus very clearly and makes it possible to assess separately the vascular nets. In low flow or no-flow areas quantification by angio-analytics shows evident *areas of no-flow* or capillary dropout. It allows quantitative assessment of capillary dropout and vascular density.

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## Neovascularization (Figure 3)

*Fluorescein angiography*: Neovascularization capillary network is concealed by early leakage in new vessels leak dye in earlier frames. The main shortcoming of dye imaging is that it identifies only exudation from NV and not NV itself. It is an indirect diagnosis that can cause errors. Nonexudative NV are not seen on FA.

Optical coherence tomography-angiography shows the finer neovascular branches and anastomoses inside the neovascular arborization or fibrous lesions. It highlights all vessels where blood is flowing. It does not depend on vessel wall leakage, it allows a better diagnosis of NV, *detecting directly both nonexudative and exudative NV* and giving a better understanding of other retinal abnormalities physiopathology. Structural OCT can identify exudation from these vessels. OCT-A gives useful information in diagnosing NV and monitoring posttreatment evolution.

Today, when we see clinical and OCT symptoms of probable or possible NV, FA is not necessary. Our first act is to perform OCT-A and we can treat with the certainty that there is pathological NV. FA and indocyanine green angiography (ICGA) may be useful in some cases, but OCT-A is replacing them in most circumstances.

*Coats disease* (**Figure 4**) *FA*: Capillary network is concealed by early leakage. OCT-A shows the finer neovascular harmonious vessels in the superficial network and the deep irregular network.

In conclusion, even if in many cases FA has been replaced by OCT-A, ophthalmologists, orthoptists, optometrists, and technicians need in many disorders to be able to interpret correctly FA imaging to reach a correct diagnosis.

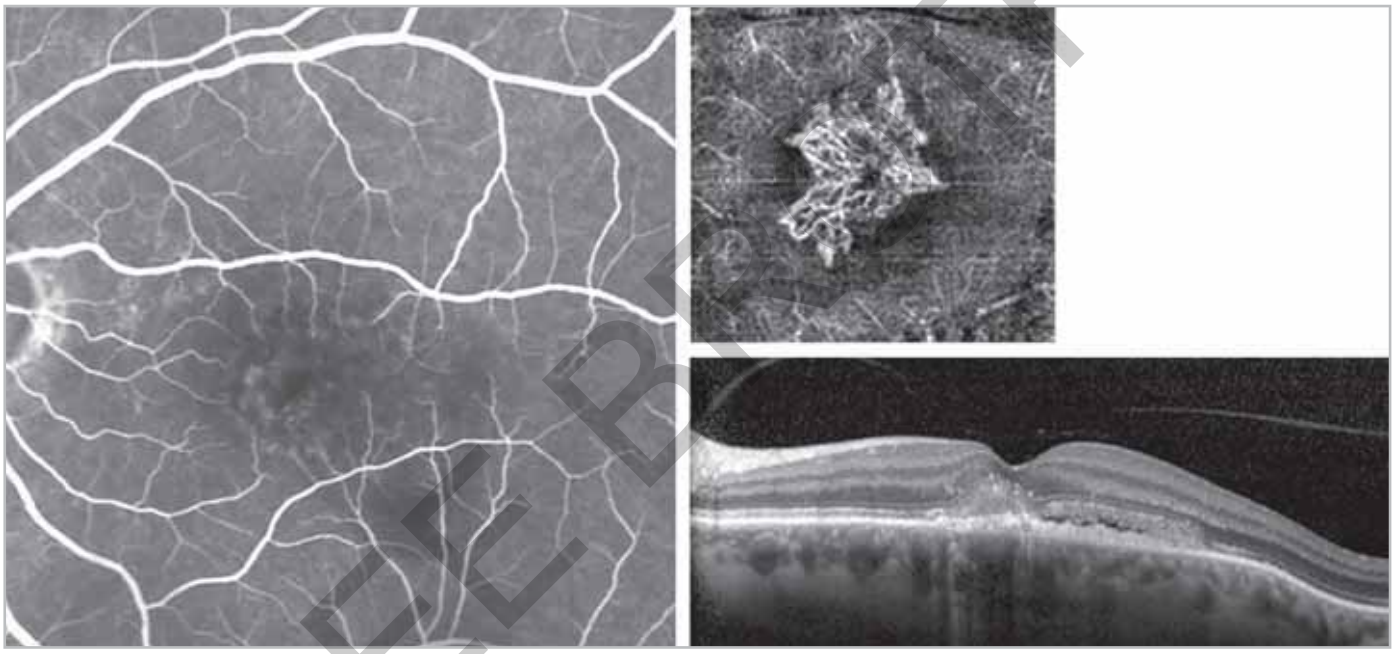


**Figure 3** Choroidal neovascularization (CNV). Fluorescein angiography in the left-hand side figure shows some light dye leakage around the CNV area. We do not see directly the new vessels but we infer their reality and location indirectly, by looking at the blurred area of dye leakage. This leakage prevents precise visualization and assessment of the new vessels. Optical coherence tomography-angiography (OCT-A) in the right-hand side figure shows directly the CNV and highlights their exact morphology. It will allow a more precise monitoring than dye angiography CNV. OCT-A imaging is more clear and more precise, and not masked by leakage. In the right-hand side figure, below we see the new vessels in the structural OCT.

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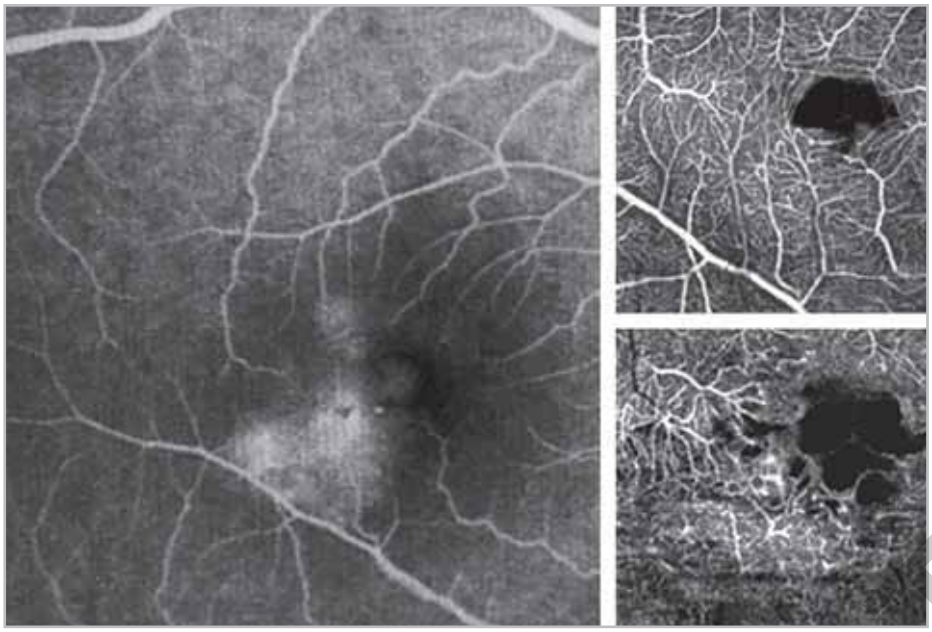


**Figure 4** Leber Coats disease. Fluorescein angiography (left hand figure) and OCT-A (right hand figures). Fluorescein angiography shows dye leakage around some retinal vascular abnormalities. Dye leakage prevents precise visualization of vascular abnormalities. OCT-A covers a smaller field but give a higher magnification. In the same posterior pole OCT-A shows superficial network (top figure) with harmonious vascular abnormalities, breaks of the vascular arcade. OCT-A bottom figure shows the deep vascular network with irregular vessels, vasodilatations. It highlights some microaneurysms. It does not show microaneurysms where blood flow is slow.
(OCT-A: optical coherence tomography-angiography)

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# Practical Handbook of Fluorescein Angiography

Fluorangiography is an established technique for the study of the retina circulation and diseases. Due to progress in clinical ophthalmology, we have expanded and completely modified the first edition, now out of stock. This new edition is completely revised and updated to bring in new technology advances. It includes new images, new chapters, and new data derived from exploration of retinal periphery and advances in optical coherence tomography (OCT) and OCT-angiography. New technology allows us to study easily with no need of manual or automatic reconstruction of the middle and far periphery.

Fluorangiography is no longer the only imaging technique in ophthalmology, but it is still a most important clinical tool, particularly with regard to the retinal periphery and inflammatory forms.

You will therefore find, in this book, our established rational method of imaging interpretation, that is, first the accurate analysis of all the elements and then the synthesis and global study of these elements, leading to deduction and diagnosis.

The standard sections are entirely restructured, and we asked specialists of the retinal periphery and eye oncology to write some completely new chapters. We present this new practical handbook to young eye specialists entering their career, but also to expert specialists wanting to update their knowledge in the progresses of imaging.

We hope that this new handbook will help residents, young, and also expert ophthalmologists in their everyday work.

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