MINERVA OFTALMOLOGICA

VOLUME 60 · No. 3 · SEPTEMBER 2018

EDIZIONI · MINERVA · MEDICA

PUBBLICAZIONE PERIODICA TRIMESTRALE - POSTE ITALIANE S.P.A. - SPED. IN A. P. D.L. 353/2003 (CONV. IN L. 27/02/2004 N° 46) ART. 1, COMMA 1, DCB/CN - ISSN 0026-4903 TAXE PERÇUE

Online version at http://www.minervamedica.it

Minerva Oftalmologica 2018 September;60(3):103-7
DOI: 10.23736/S0026-4903.18.01805-6

REVIEW

OCT ANGIOGRAPHY: A NEW ERA OF OPHTHALMOLOGY

Myopic choroidal neovascularization and OCT angiography

Alfredo PECE *

Centro Oftalmologico Retina 3000, Milan, Italy

*Corresponding author: Alfredo Pece, Centro Oftalmologico Retina 3000, Milan, Italy. E-mail: pece.retina@mclink.it

ABSTRACT

Myopic choroidal neovascularization (CNV) is one of the most frequent causes of visual impairment and legal blindness in the world, especially among Asians. Its diagnosis of myopic CNV ranges from fundus biomicroscopy to multimodal imaging — which includes retinal fluorescein angiography (FAG), — from spectral domain structural optical coherence tomography (OCT) to OCT angiography. FAG shows early hyperfluorescence of the vascular lesion with poor leakage in 80%, or more evident leakage in 20% of cases. OCT examinations have reached a very high technological level and a very-high image resolution. In the diagnosis of CNV, it is essential to exclude vitreous-retinal tractions that are often present at the posterior pole, or other syndromes such as dome-shaped macula and tilted disc syndrome. Retinal fluorescein angiography is currently the gold standard, although it is not always easy to identify CNV, as leakage is sometimes missing, and it can be confused with atrophy-associated areas. This review illustrates and compares the main diagnostic tools which are currently used for CNV identification.

(*Cite this article as:* Pece A. Myopic choroidal neovascularization and OCT angiography. Minerva Oftalmol 2018;60:103-7. DOI: 10.23736/S0026-4903.18.01805-6)

KEY WORDS: Choroidal neovascularization - Fluorescein angiography - Microscopy - Optical coherence tomography - Diagnostic imaging.

Myopic choroidal neovascularization (CNV) is one of the most frequent causes of visual impairment and legal blindness in the world, especially among Asians. Numerous changes occur in the fundus in degenerative myopia up to CNV, a fairly frequent event in clinical practice affecting about 30% of subjects with pathological myopia greater than 6D with an axial length greater than 26 mm. The diagnosis of myopic CNV ranges from fundus biomicroscopy to multimodal imaging — which includes retinal fluorescein angiography (FAG), — from spectral domain structural optical coherence tomography (OCT) to OCT angiography (OCT-A). FAG shows early hyperfluorescence of the vascular lesion with poor leakage in 80%, or more evident leakage in 20% of cases. OCT examinations have reached a very high technological level and a very-high image resolution. In its latest version, OCT has a speed of 70-100,000 scans per second and great image quality. In the diagnosis of CNV, it is essential to exclude vitreous-retinal tractions that are often present at the posterior pole, sometimes with the presence of macular microholes, or so-called benign hemorrhages, namely not accompanied by CNV, or more difficult syndromes such as the dome shaped, or the tilted disk syndrome. At present, retinal fluorescein angiography remains the gold standard, but it is not always easy to identify CNV accurately. Indeed, leakage is sometimes missing and can be confused

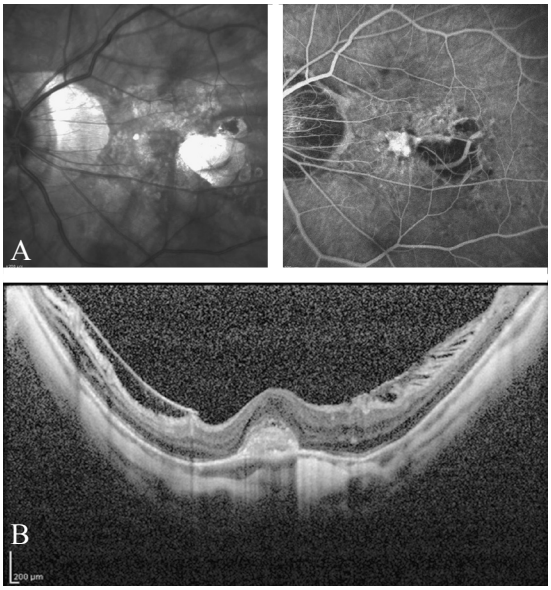

Figure 1.—A) Retinography and fluorescein angiography clearly show a neovascular lesion. B) OCT highlights the hyper-reflectivity area typical of CNV.

with atrophy-associated areas that appear difficult to differentiate (Figure 1, 2, 3, 4).[1-7]

The main features of myopic CNV as seen by fluorescein angiography are:

- type 2 CNV above the pigmented epithelium;
- usually small dimensions;
- generally modest leakage;
- impregnation of the dye from the early stages but sometimes at more advanced stages, too;
- sometimes presence of pigment or fibrosis (older forms).

Spectral domain structural OCT with B-scan allows us to clearly identify the presence of CNV as the presence of an area of hyper-reflectivity often associated with edema and retinal detachment. OCTs are sometimes not easy to perform because of aberrations due to the non-homogeneous elongated bulb, limited choroidal thickness, difficulties in fixation, or opacity. In some cases, it is best to perform this after dilating the pupil. However, there is good agreement between OCT and the presence of CNV.

The main features of myopic CNV as seen by OCT are:

- area of hyper-reflectivity, usually of moderate size and dome-shaped;

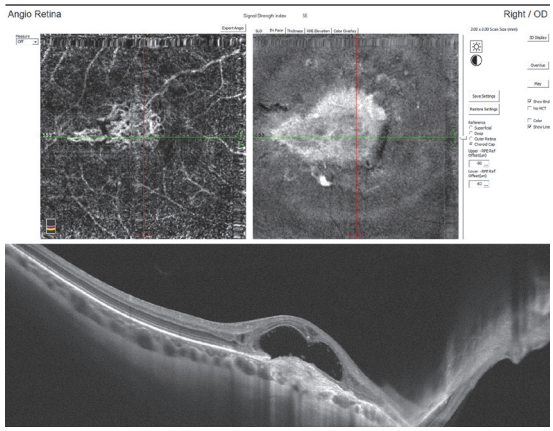

Figure 2.—*En-face* OCT-A and OCT of a myopic CNV with visualization of the neovascular texture inside the CNV.

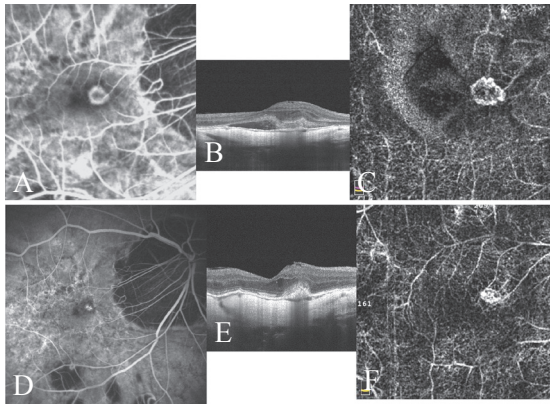

Figure 3.—Fluorescein angiography shows a macular neovascular lesion before (A) and after treatment with intravitreal injections (D). OCT-A shows the vascular texture of the pre- (C) and post- (F) intravitreal CNV injection. B, E) OCT images before and after treatment.

- lesion with "fuzzy" edges;
- thickening of the corresponding retina;
- involvement of external segments;
- CNV is often well delimited but the margins are sometimes poorly defined;
- presence of fluid or limited and unclear retinal cysts (50% of cases);
- differential diagnosis possible with retinal bleeding;
- chance of false negatives.

As mentioned, both the fluorescein angiography and OCT exams, if well conducted, allow us to diagnose CNVs with precision in the majority of cases. It is however true that we have cases in which the hyperfluorescent areas of FAG do not

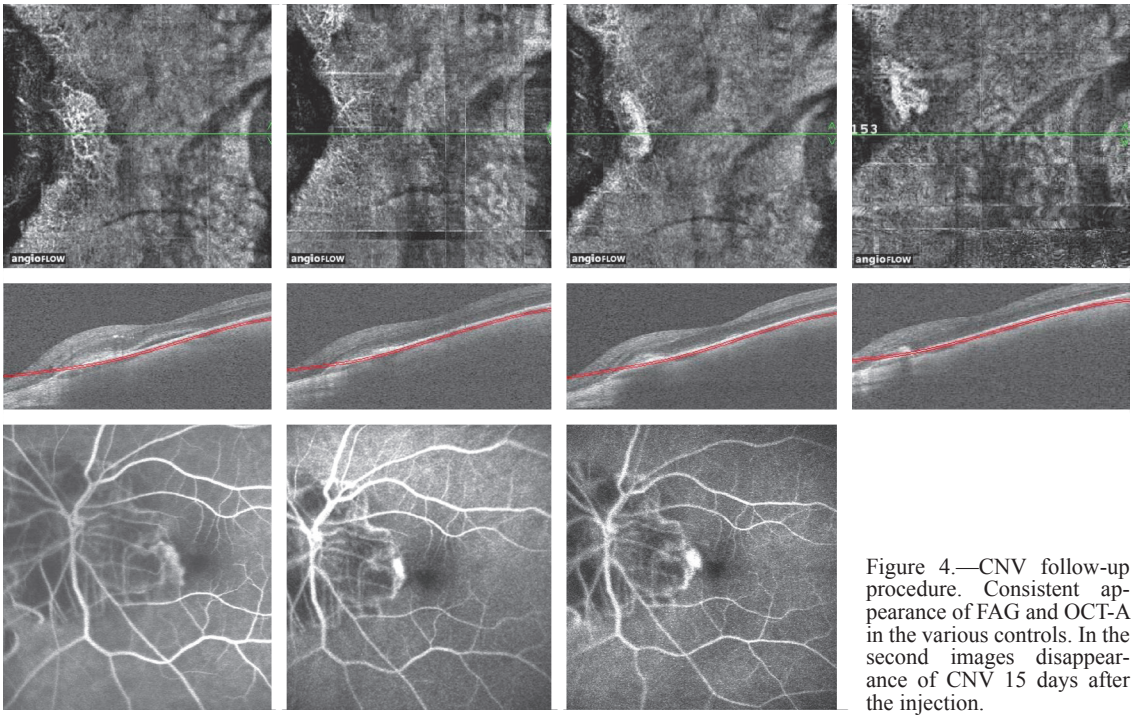

Figure 4.—CNV follow-up procedure. Consistent appearance of FAG and OCT-A in the various controls. In the second images disappearance of CNV 15 days after the injection.

allow clear identification of CNV, cases in OCT that are not clearly interpretable, and cases of intolerance or contrast allergy. OCT-A is a recently introduced diagnostic methodology that has already taken its place as an important examination in the diagnosis and in the follow-up of CNV including after intravitreal injections. OCT-A is a non-invasive, non-contrast, *en-face* technique that provides three-dimensional images of perfusion, *i.e*. of flow at the various levels studied. The OCT-A image is based on the scattering of signals detected by the movements of vascular cells in blood vessels. The great advantage of this method is not only that there is no contrast agent but also that the images of the CNV vessels are significantly better than after using FAG.

The advantages of using OCT-A in the diagnosis of myopic CNV are:

- better definition of the vascular network;
- improved visualization of structure, interconnections and anastomoses;
- very good agreement with fluorescein angiography;
- possibility of measuring the neovascular area;
- site identification;
- possibility of automatic comparison with previous exams;
- examinations done frequently;
- absence of intravenous contrast;
- economic savings.

The main disadvantages of using OCT-A in the diagnosis of myopic CNV are:

- not always easy to identify the network;
- not available in case of no fixation or poor visus;
- problem with evaluating neovascular activity and flow rate of CNV;
- projection artefacts.

How often do you achieve a positive OCT-A examination?

We examined 40 eyes of 40 consecutive patients with pathological myopia and the presence of CNV. The equipment used was Avanti (RTVue XR Avanti; Optovue Inc, Fremont, CA, USA). The neovascular network was visualized with precision and reproducibility in 60% of patients in miosis, in 80% of cases in mydriasis. The rate of undetected CNVs reported ranges from 11% to 26%.

Practical advice

The use of OCT-A is more challenging in case of lack of fixation and low visus. Particular attention must be paid in performing the examination, which sometimes has to be repeated several times, preferably in mydriasis. The equipment used is important. The more advanced OCT-A systems with control and repair of motion artifacts often provide a better-defined image.

What does a vascular network look like?

The morphology of CNV, the core of CNV (present or otherwise) and its margins (defined or not) are currently evaluated. As is shown below a distinction has been made by Querques *et al.* between "interlacing" indicating a more active form, and "tangled" which is less active. After the injections there is often a remodeling of the lesion, with transit from the first to the second form.[1]

How does a vascular network change after anti-VEGF drug injection?

The vascular lesion visualized at OCT-A changes after intravitreal injection. Vascular anastomoses between the various capillary plexuses and the various planes tend to a decrease and at times disappear. The larger and more "mature" vascular trunks remain, often the expression of a chronic lesion or, in any case, the onset of a more active and more aggressive lesion.

Practical advice

After the injection it is useful to verify the morphology of the vascular network with OCT-A to evaluate both the effectiveness of the therapy and to have an image of the vascular network and compare it with that of the pre-injection. OCT-A is recommended after 15, 30, and 45 days, and less frequently from then on. This allows the reopening of the lesion to be evaluated without carrying out fluorescein angiography.

Vascular flow analysis with OCT-A

Due to its intrinsic ability to document choroidal and retinal circulation in vivo, OCT-A also makes it possible to analyze even minimal changes at macular and peripapillary levels. The advantage in such cases is good repeatability and reproducibility of the examination. Both superficial and deep macular flow densities and peripapillary capillary network decreased in pathological myopia with a negative correlation with the axial length, while there is a positive correlation between these parameters and visual acuity.

Fluorescein angiography and OCT-A

We compared 20 eyes with naïve myopic vascular CNV. Fluorescein angiography revealed the neovascular lesion in all cases. OCT-A could not be evaluated in four patients, in the 16 patients whose examination was of good quality, OCT-A showed the vascular network in all cases.

Practical advice

Although fluorescein angiography represents the gold standard in detecting myopic CNV, the result with OCT-A has been absolutely comparable when it has been possible to carry it out. In such cases OCT-A is a viable and accurate alternative to fluorescein angiography, and needs to be considered in view of its speed, cost and absence of side effects.

Evidence synthesis

In the study by Querques *et al.*,[1] 36 eyes of 28 consecutive patients with myopic CNV were included. In 4 out of 36 eyes it was not possible to classify the CNV "shape," "core," "margin," and "appearance" because the vascular network was not clearly visualized due to the poor quality of the examination. CNV shape on OCT-A was rated as circular in nine eyes and irregular in 23 eyes. CNV core was visible in 11 eyes. CNV margin was considered as well defined in 16 eyes and poorly defined in 16 eyes. CNV appearance showed an "interlacing" aspect in 16 eyes and a "tangled" aspect in the other 16 eyes. A total of 11 CNVs were defined as active, nine of which (81.8%) were interlacing, while a total of 21 were inactive, 14 of which (66.7%) were tangled. OCT-A sensitivity turned out to be 90.48% and specificity was 93.75%.

We describe the OCT-A features of myopic CNV secondary to pathological myopia and demonstrate its high sensitivity and specificity for neovascular detection. Qualitative evaluation of OCT-A characteristics may allow one to recognize different patterns, possibly corresponding to different degrees of neovascular activity.

Al-Sheikh *et al*.[3] evaluated the retinal capillary microvasculature and the choriocapillaris in myopic eyes using quantitative OCT-A analysis. The density of the retinal capillary microvasculature is reduced and the area of flow deficit in the CC is increased in eyes with greater myopia.

Liu *et al*.[4] used OCT-A to study cases of myopic or idiopathic CNV. OCT-A demonstrated details of reduction of CNV size and vessel density simultaneously. OCT-A could demonstrate the valid CNV form having advantages of rapid, noninvasive and repeatable. Combination of OCT-A and other examinations had a promising future of clinical application on ocular neovascularization diseases. Further studies with larger sample size and longer follow-up are necessary and more advanced OCT-A is being expected.

The study by Miyata *et al*.[2] aimed to assess whether OCT-A can be used as an alternative to conventional fundus fluorescein angiography (FFA) for the detection of myopic choroidal neovascularization (CNV).

Conclusions

OCT-A is a new imaging technique that makes it possible to evaluate blood flow and reconstruct an angiography map of the macular region and in particular of CNV. In pathological myopia, precisely because of the intrinsic characteristics of CNV and the anatomical retinal conditions, OCT-A is highly sensitive for identifying CNV and detecting vascularization characteristics in even greater detail than with fluorescein angiography. In addition, the ability to follow the lesion over time allows us to detect early signs of reactivity after intravitreal injections. In view of the rapidity of the examination and the absence of side effects, it can be considered as an option in all cases of myopic CNV and sometimes also as an alternative to fluorescein angiography.

Our results indicate that OCT-A can detect most myopic CNVs if high-quality images are acquired and can preclude the requirement for FFA in these settings.

References

1. Querques L, Giuffrè C, Corvi F, *et al.* Optical coherence tomography angiography of myopic choroidal neovascularization. Br J Ophthalmol 2016.

2. Miyata M, Ooto S, Hata M, Yamashiro K, Tamura H, Akagi-Kurashige Y, *et al.* Detection of Myopic Choroidal Neovascularization Using Optical Coherence Tomography Angiography. Am J Ophthalmol 2016;165:108–14.

3. Al-Sheikh M, Phasukkijwatana N, Dolz-Marco R, Rahimi M, Iafe NA, Freund KB, *et al.* Quantitative OCT Angiography of the Retinal Microvasculature and the Choriocapillaris in Myopic Eyes. Invest Ophthalmol Vis Sci 2017;58:2063–9.

4. Liu B, Bao L, Zhang J. Optical Coherence Tomography Angiography Of Pathological Myopia Sourced and Idiopathic Choroidal Neovascularization With Follow-Up. Medicine (Baltimore) 2016;95:e3264.

5. Milani P, Pece A, Pierro L, Bergamini F. Imaging of naive myopic choroidal neovascularization by spectral-domain optical coherence tomography. Ophthalmologica 2014;232:28–36.

6. Mo J, Duan A, Chan S, Wang X, Wei W. Vascular flow density in pathological myopia: an optical coherence tomography angiography study. BMJ Open 2017;7:e013571.

7. Milani P, Montesano G, Rossetti L, Bergamini F, Pece A. Vessel density, retinal thickness, and choriocapillaris vascular flow in myopic eyes on OCT angiography. Graefes Arch Clin Exp Ophthalmol 2018.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Manuscript accepted: July 12, 2018. - Manuscript received: July 10, 2018.