

# Optic coherence tomography-angiography – a new technique in the diagnosis and follow-up of the patients with age-related macular degeneration – an overview

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## Summary

Age-related macular degeneration (AMD) is a degenerative, progressive disease, which destroys the central retina. AMD has two main forms - „dry“ and „wet“ (exudative). In order to make the diagnosis of AMD with CNV, apart from ophthalmoscopy, specialized tests are needed - fluorescein angiography (FA), indocyanine angiography, OCT, OCT-angiography (OCT-A). OCTA is a new and non-invasive technology. Compared to the old, well-known techniques for retinal evaluation, it is very precious because of its high resolution and detailed images – which allow early diagnosis and objective monitoring of the lesions in the future. The aim of this review is to describe the principles of function, features of the device and its application in everyday clinical practice in diagnosing patients with macular pathology. A systematic search of the literature, published in the past decade was identified from PubMed and Ovid databases with reference to the Preferred Reporting items for Systematic Review. AMD is a disease that is increasingly socially important because of the aging population in developed countries. The increasing use of OCT-A nowadays suggests new classification systems. The non-invasiveness, the short examination time and the high informativeness that OCT-A brings in relation to AMD requires a deeper study of the methodology and the development of new classifications to facilitate clinical practice.

**Key words:** Age-related macular degeneration, application, choroidal neovascularization, OCTangiography

## Introduction

Age-related macular degeneration (AMD) is a degenerative disease, which affects the central retina and progresses over time. The disease is among the leading causes of blindness worldwide (Wang et al. 2007; Pascolini and Mariotti 2011; Weiner et al. 2011; Klein et al. 2013) and ranks third after cataract and glaucoma (Leske et al. 2006). AMD is subdivided into two main forms - „dry“ and „wet“ (exudative). Regardless of its form, it leads to irreversible visual function loss and worsens patients' life quality (Leske et al. 2006). The main



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characteristic of 'wet' AMD is the choroidal neovascularization (CNV), which, if untreated, is associated with severe vision loss due to bleeding and exudation. Until the introduction of anti-vascular endothelial growth factor (anti-VEGF) injections for intravitreal administration in 2007, AMD with CNV was considered the more severe form, because the neovessels are with incompetent vessel wall and are predisposed to bleeding and exudation, resulting in fast visual loss. In order to make the diagnosis of AMD with CNV, besides ophthalmoscopy, specialized tests are needed - fluorescein angiography (FA), indocyanine angiography, OCT, OCT-angiography (OCT-A).

## Aim

The purpose of this review is to describe the OCT-A, as a newly developed technological tool, the features of the device and its application in everyday clinical practice in diagnosing patients with macular pathology.

## Materials and methods

A systematic search of literature, published in the past 10 years in PubMed and Ovid databases with reference to the *Preferred Reporting items for Systematic Review* was made. The predefined selection inclusion criteria were clinical applications of OCT-A in relation to diagnosis. The keywords used were OCT-A, macular degeneration, choroidal neovascularization, follow-up.

## Discussion and results

FA is still the gold standard in diagnosing retinal diseases. FA has undeniable capabilities of visualizing important microvascular details, but dye injection is required. The administration of contrast can be associated with potentially severe and even life-threatening adverse reactions (Gess et al. 2011). OCT and OCT-A are recently developed medical technical devices, which are extremely useful in everyday clinical practice for fast, non-invasive and objective monitoring of retinal lesions (Anger et al. 2004; Spaide et al. 2008; Adhi and Duker 2013).

OCT-A was first demonstrated back by Chinn et al. in 1997 (Enfield et al. 2011). In 1997, the quality of images obtained was still poor and the device did not find place in everyday clinical practice. In the following decade, the imaging technology evolved and in 2006 Makita et al. presented the first contemporary OCT-A device, based on detecting movement of the formed elements of the blood as they pass through the vessels, without introducing a dye (Potsaid et al. 2010). Since 2007, several OCT-A methods have been described to create a three-dimensional contrast-free map at the microcirculatory level. A historically used method is signal-to-noise ratio (SNR) to detect blood flow (Grulkowski et al. 2012). In the last few years, the decorrelation principle has been used, modified by different companies. The OCT signal is first split into several (most often four) spectral beams. Thus, instead of obtaining one image with a high resolution, several with a lower one are obtained. Lower axial resolution implies higher coherence to the blood cell reflected signal, thus increasing contrast (Fingler et al. 2007). The contrast between static and dynamic tissues is generated by calculating the signal amplitude decorrelation between repeated, consecutive

B-scans in the same section. Each spectral beam yields a different pattern, giving independent information about the blood flow. The signal is boosted by summarizing the amplitude of decorrelation patterns of many spectral beams. The lower axial resolution is also a method of correcting the artifacts produced by axial eye movements (resulting from retrobulbar pulsations).

OCT-A represents retinal blood flow divided into two superficial and deep plexuses (Vakoc et al. 2009). Thus, the device allows imaging classic and occult neovascular membranes. Classical anatomical studies from the beginning of the twentieth century showed that the distribution of retinal vessels is organized into three layers (Blatter et al. 2012):

1. Superficial of large and medium-sized vessels in the layer of retinal nerve fibres. It can be observed with an ophthalmoscope.
2. Internal plexus – small capillaries located on the surface of the inner nuclear layer.
3. External plexus - morphologically identical to the internal but located on the surface of the external plexiform layer.

OCT-A demonstrates these layers *in vivo* and allows the study of the two vascular plexuses separately. This makes it possible for the ophthalmologist to better assess the level of impairment, because the FA image is cumulative and the two plexuses overlap. The superficial and deep plexus can be differently affected by a pathological process.

One of the main advantages of this technology is the opportunity to visualize the different plexuses separately and without the introduction of intravenous dye. When analysing an OCT-A image, an ophthalmologist should always take into consideration the depth of the scan and try to describe the image, based on reflectivity, current, morphology and architectonics.

When interpreting an OCT-A image, the plexuses in four scanning depths (Souied et al. 2016) are divided into superficial vascular plexus, deep vascular plexus, RPE/Bruch's membrane complex, and choroid. In order to make sure that the clinical correlation is correct, one should always define the scanning depth.

For each of the four scanning depths, additional characteristics should be determined:

- Decorrelation and flow characteristics. OCT-A generates an image through the contrast obtained during the movement of the blood formed elements. Blood flow can be slow or fast, its direction – transverse or vertical, and the vessels - thin or thick.
- Vascular morphology and architectonics. The architecture of the vascular network can be regular or irregular; dense, scanty, dilated. Loops, vessel shape and capillary density are also evaluated. A cross-section shows the shape of the capillaries and their size.
- Texture is a new term for OCT-A, which is not used in classic OCT or in FA. It is determined by vascular density (Farecki et al. 2017).

The classification of the choroidal neovascularization, based on the FA-images is the gold standard for evaluating the patients. It is widely used, simple and accurate at the same time. The most common is the Type 1 of CNV: it starts

from the choroid and reaches Bruch's membrane and RPE. The Type II CNV is located under the retina (subretinally). Intraretinal neovascularization Type III is also known as retinal angiomatous proliferations (RAP) and it is very rare.

The wide introduction of the OCT-A in everyday clinical practice has led to the necessity of creating new classifications of the CNV, based on the OCT-A images.

The first to report the application of OCT-A in the early detection of type I CNV were Palejwala et al. Various publications have reported on the technical abilities of OCT-A to also detect type II (El Ameen et al) and type III CNVs.

Because OCT-A is becoming a first choice tool for control and follow-up the progression and treatment results in patients with retinal pathology related to its noninvasive approach, the necessity of new descriptive term and classification increases.

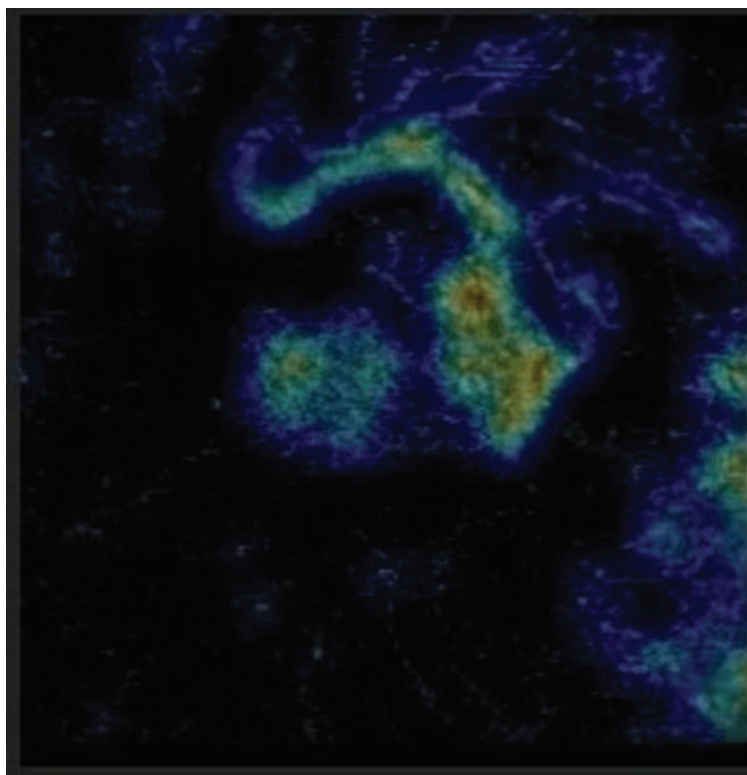
A French group of researchers from Creteil Hospital, examined 80 eyes with neovascular AMD. Based on the images of OCT-A, Prof Coscas and his team divided CNV in six different classes: „seafan“, „medusa“, „dead tree“, „lace“, „filaments“, „indeterminate „ (Kuehlewein et al. 2015; Miere et al. 2015).

The 'seafan' type CNV presents with a massive truncus with eccentric feeding vessel and thin capillary ramifications (Fig. 1).

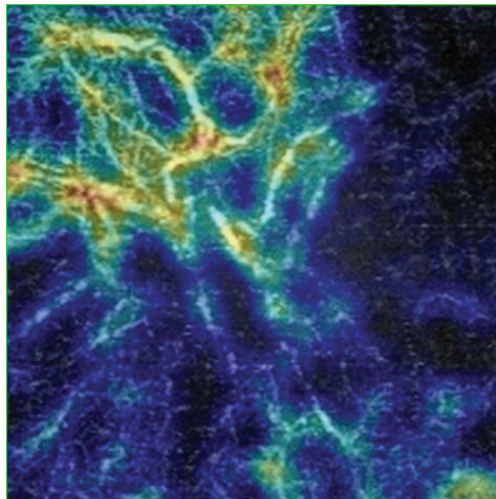
The „gorgon“ type CNV consists of a central feeding vessel with centrifugal vascular trunci with thin capillaries and circular peripheral anastomoses surrounded by a dark halo (Fig. 2).

The „dead tree“ type of CNV is characterized by a massive main truncus and ramifications varying in size and caliber (Fig. 3).

The „lace“ type of CNH demonstrates an anastomosing vascular network, without a major vessel (Fig. 4).

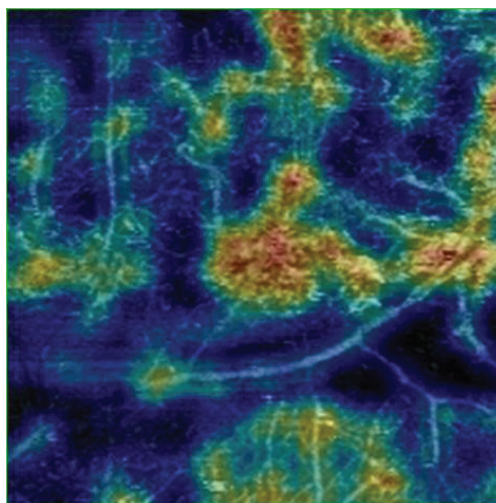


**Figure 1.** CNV "seafan" – own archive, Eye Clinic "Zrenieto" – Prof. Tanev's Team, Sofia, Bulgaria.



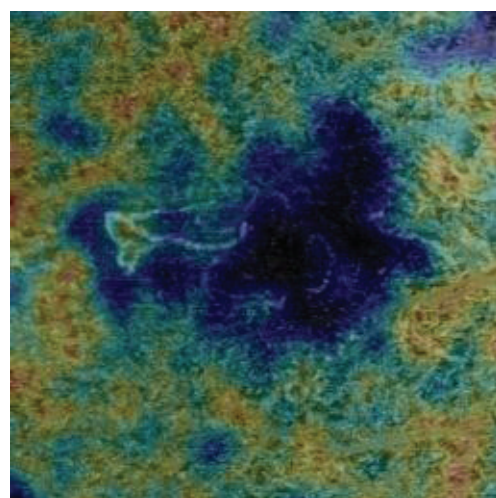
**Figure 2.** CNV "Gorgon" - own archive, Eye Clinic "Zrenieto" – Prof. Tanev's Team, Sofia, Bulgaria.

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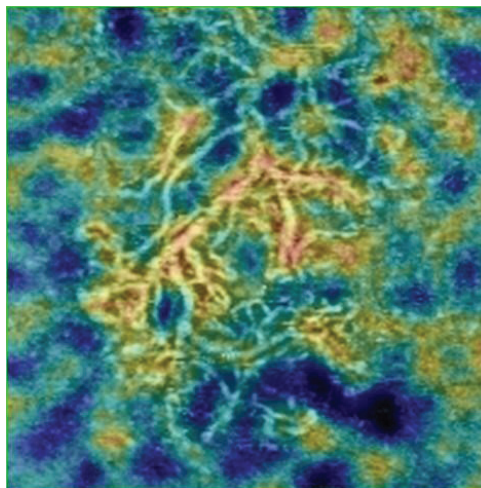
**Figure 3.** CNV "Dead tree" - own archive, Eye Clinic "Zrenieto" – Prof. Tanev's Team, Sofia, Bulgaria.

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**Figure 4.** CNV "Lace" - own archive, Eye Clinic "Zrenieto" – Prof. Tanev's Team, Sofia, Bulgaria.

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**Figure 5.** CNV “Filaments” - own archive, Eye Clinic “Zrenieto” – Prof. Tanev’s Team, Sofia, Bulgaria.

Filamentous CNV is composed of multiple intertwining filamentous vessels (Fig. 5). CNV, which cannot be attributed to the described morphological forms, is classified as „indeterminate“.

All morphological variants are the object of scientific interest from the point of view of their potential role as markers for the progression of AMD. Furthermore, once identified by OCT-A, they can be used as a baseline to follow vascular remodeling and the effect of intravitreal administration of anti-VEGF, which is currently the gold standard for the treatment of the exudative form of AMD.

## Conclusion

AMD is a disease that is gaining more and more social importance due to aging of the population in developed countries. The non-invasiveness, the short time of examination and the high informativeness that OCT-A brings in relation to AMD requires further study of the methodology and the development of new classifications to facilitate clinical practice.

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