



## Clinical application of the peripheral retinal angiography

Monika J. Turczyńska, Przemysław Krajewski, Daria Kęćik, Dariusz Kęćik

Infant Jesus Clinical Hospital University Clinical Center, Medical University of Warsaw, Warsaw, Poland

### ABSTRACT

In clinical practice, the posterior pole area is assessed more often than the periphery retina. Fluorescein and indocyanine green angiography (FA and ICGA), optical coherent tomography (OCT), and more recently OCT angiography (OCTA) are standard in the assessment of retinal diseases. OCT and OCTA are currently only used to assess changes in the posterior pole. The authors present their own experience gathered during in the last 15 years of performed angiographic tests of the retina using the following apparatus: FF450 Zeiss, Optos 200Tx and Spectralis HRA + OCT with a 102° wide-angle lens. The authors draws attention to the diagnostic value of wide-field angiography in selected retinal vascular diseases: diabetic retinopathy, retinal vein occlusion, retinal

artery occlusion, Susac syndrome, peripheral retinal vascular malformations. They also discuss the use of peripheral angiography in inflammatory diseases of the retina and choroid, white-spot syndromes, nevi and tumors. The authors' own experience indicates the value of performing additional angiograms of the peripheral retina during the assessment of macular diseases, which can highlight changes that often require further diagnostic and therapeutic procedures.

**SŁOWA KLUCZOWE:** diabetic retinopathy, vasculitis, retinal vein occlusion, retinal artery occlusion, peripheral retinal angiography, wide-field angiography.

### INTRODUCTION

Peripheral retina is a site for pathological changes in multiple ocular diseases causing visual impairment or loss. Diagnostic imaging has played a very significant role in ophthalmology for a long time. After the first photograph of the human retina was taken in 1886, the real breakthroughs came with the introduction of fluorescein angiography (FA) in the early 1960s [1] and indocyanine green angiography (ICGA) in the 1970s [2]. Two decades later, both diagnostic procedures became the standard in ophthalmic imaging of retinal vascular conditions, mainly in the posterior pole. The far peripheral retina was inaccessible for FA- and ICGA-based diagnostic assessment for many years.

### ANGIOGRAPHIC EXAMINATIONS

Angiography is an invasive procedure which requires the patient's written consent. It involves intravenous injection of a dye and taking a series of photographs of the anterior or posterior segments of the eye. Angiography is a suitable modality for the morphological (anatomical) assessment of the eyeball structures and functional (dynamic) analysis of blood circulation in the posterior segment, in the retinal and choroidal vessels. In ophthalmology ap-

plications, the phenomenon of dye fluorescence (fluorescein sodium and indocyanine green) is used, consisting in the emission of light at a higher wavelength with excitation of the dye with light of a shorter wavelength.

Fluorescein has a low molecular weight (376.67 Da), and binds to blood albumins in approximately 80%. Also, under normal conditions, it does not pass through the vessel walls in the retina and the central nervous system [3]. Of note, leakage of the contrast agent beyond the vessel lumen indicates a pathological process and breakdown of the inner blood-retinal barrier. Protein-unbound fluorescein prevents the assessment of large choroidal vessels, as it passes rapidly through the fenestrations of the choriocapillaris and spreads under the retinal pigment epithelium (RPE). FA is used for imaging and evaluating normal or pathological vessels, mainly in the retina and choriocapillaris [3–6], but it is also suitable for visualizing the vessels of the iris and conjunctiva, and pathological corneal vessels [7].

Indocyanine green is twice the molecular size of fluorescein (775 Da), and binds to blood proteins (primarily alpha-1 lipoproteins) in 98%. In addition, it practically does not penetrate the walls of the choriocapillaries. ICGA is used primarily for the assessment of abnormalities located at the choroidal level [4].

### CORRESPONDING AUTHOR

Monika J. Turczyńska, MD, PhD, Infant Jesus Clinical Hospital University Clinical Center, Medical University of Warsaw, 4 Lindleya St., 02-005 Warsaw, Poland, e-mail: mturczynska@komt.pl

Angiography is contraindicated in patients with allergy to the contrast agent, which is extremely rare nowadays. Similarly to other imaging techniques used in ophthalmology (except for ultrasonography), angiographic evaluation is impossible to perform with opaque optical media.

Conducting an angiographic examination, especially of the peripheral retina, requires good patient cooperation. The person examined must fixate properly, refrain from clenching the eyelids, and follow the verbal instructions of the examiner. The examination may be more challenging in patients with nystagmus, ptosis, deep orbits, and eyelashes obscuring the image.

## WIDE-ANGLE AND ULTRA-WIDE-ANGLE IMAGING

One of the goals in the development of novel technologies is to achieve the widest possible field of view (FoV) of retinal images. In the first fundus camera designed by Carl Zeiss Company in 1926 the FoV was 20°. In subsequent years, retinal imaging over a 30° FoV became the standard, enabling the assessment of the retinal area between the temporal vascular arches. Further advances in ophthalmic technology offered an option to use lenses with an imaging FoV of up to approximately 50° to assess the posterior pole of the eye (a circle equal to 5 diameters of the optic nerve disc from the macular center). They have been in use since then. Other techniques employed over the years consist of combining multiple fragments of peripheral retina photographs – 7 standard fields (7SF), 3 fields covering the posterior pole and 4 showing individual quadrants, in order to compile one image representing part of the peripheral retina (so-called composite photographs). 7SF imaging made it possible to visualize the retina over a FoV of approximately 75°, i.e. an area covering approximately 30% of the total retinal surface [8]. Such montage techniques are very useful for static examinations (color images), but have their limitations in dynamic imaging due to the rate of dye flow through different parts of the peripheral retina. Since photographs are taken at different stages of the examination, for technical reasons it is difficult to assemble them into a single diagnostic image [9]. It must be noted that with traditional fundus cameras the imaging of peripheral retina required appropriate technical skills, patience, and patient cooperation.

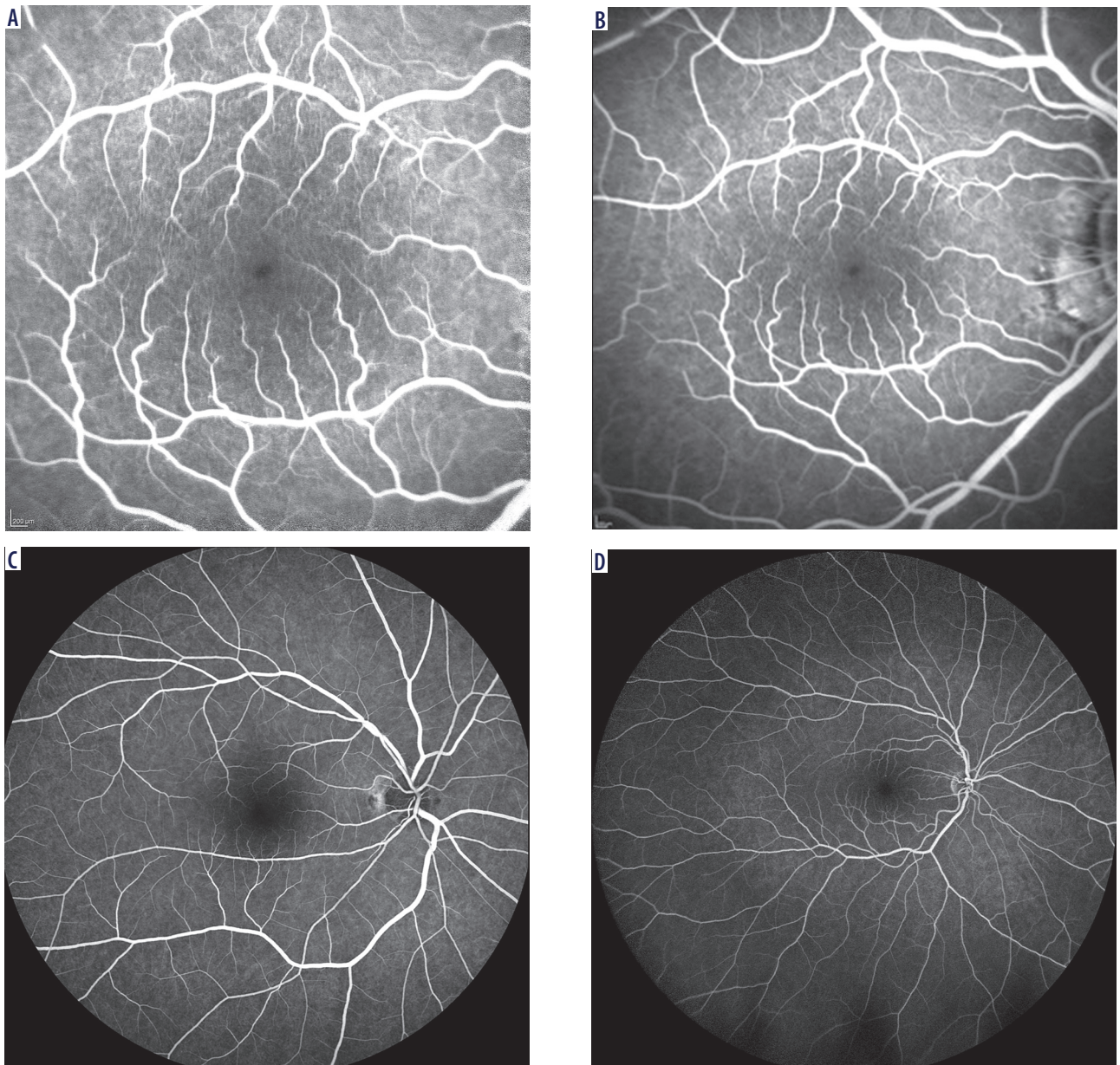
The first commercial imaging device, Optos PLC (Scotland), was introduced into clinical practice in 2009. In the subsequent years, wide-angle systems were improved and nomenclature was introduced. In 2019, Choudhry *et al.* proposed terminology for the field of view captured by retinal imaging based on the visible eye fundus structures. Wide-field image of the eye fundus is defined as a single-capture image, centered on the fovea, capturing the elements of the retina up to the line of convergence of four vortex veins, covering a view of 60°–100°. In contrast, ultra-wide-field image of the eye fundus is defined as a single-capture image, centered on the fovea, capturing the elements of the retina going beyond the line of convergence of four vortex veins, covering a view

of 100°–220°. The term “panretinal” was also proposed to refer to the imaging of the entire retina (360°), though there is as yet no clinically available technology to capture a single image covering such field of view [10].

The development of scanning laser ophthalmoscopy (SLO) has made it possible to employ UWF for visualizing the periphery of the retina by capturing a single wide-field image (Optos PLC, Dunfermline, UK) [9, 11]. Notably, such images are obtained without using any additional instrumentation (e.g. lenses), and do not require pupil dilation. Also, with appropriate patient cooperation and mydriasis, the field of view of the image can reach as far as the retinal ora serrata. The Optos system (e.g. Optos 200Tx) makes use of an ellipsoidal mirror and appropriate positioning of the laser beams, which together allow wide scanning angles. In addition, the combination of lasers of different wavelengths (green – 532 nm, red – 633 nm) yields a wide range of images including red-free, infrared, autofluorescent (AF) and pseudo-color. The design of the Optos 200Tx ophthalmoscope is suitable for obtaining FA and ICGA images over a 200° field of view (82% of the retina visualized in a single image). However, the Optos system also has a number of disadvantages including peripheral distortions and eyelid and eyelash artifacts, lack of possibility to visualize the entire peripheral retina, unrealistic color images, and lower resolution within the posterior pole compared to the „high resolution” SLO ophthalmoscope Spectralis (Heidelberg Engineering, Inc., Heidelberg, Germany) [9, 12].

Spectralis HRA + OCT (Heidelberg Retina Angiograph + Optical Coherence Tomography) laser scanning system is a non-contact instrument designed for imaging the retina and the anterior segment of the eye. It is equipped with additional software tracking the same fragments of the retina in order to obtain greater accuracy which is useful, for example, in non-compliant patients, or individuals with cataracts or nystagmus. Other highlights of the system include image overlaying and averaging functions designed to produce an improved signal-to-noise ratio and hence optimize the quality of images. Changing the imaging field in Spectralis is done by using one of the interchangeable lenses: 30° (imaging in 15°, 20° and 30° fields of view), 55° (imaging in 25°, 35° and 55° fields of view), 102° wide-angle lens (imaging in 51°, 68° and 102° fields of view) (Figure 1). With correct positioning of the eyeball and good patient cooperation, it is possible to visualize the retina up to the ora serrata. However, unlike Optos Tx200, Spectralis provides no option to obtain a single ultra-wide-angle photograph. Another disadvantage of SLO Spectralis is the fact that no image of the peripheral retina can be produced in patients with excessively deep orbits [9, 12].

It is important to note that in SLO-based angiography systems smaller doses of fluorescein and indocyanine green are needed to obtain angiograms of comparable quality to traditional fundus cameras based on digital flash photography<sup>13</sup>. Benefits of the currently available angiography systems include digital image processing technologies and the possibility to conduct examinations at a narrow pupil (ap-



**Figure 1.** Imaging areas. Spectralis HRA + OCT. **A)** 20°, **B)** 30°, **C)** 55°, **D)** 102°

proximately 2 mm). This feature is particularly beneficial in patients whose pupils do not dilate in response to mydriatics or in whom pupil dilation is contraindicated.

Ultra-wide-angle imaging has a very important role in ophthalmic diagnostics. Changes secondary to vascular disorders are located both in the posterior pole and in the peripheral retina. In some cases, abnormalities that support the diagnosis of a given condition – or the initiation of appropriate treatment – are located solely in the far periphery, and their visualization and evaluation before the advent of wide-field angiography were challenging or outright impossible. Leder et al. reviewed data from 23 patients with non-infectious retinal vasculitis over a course of 71 visits. Based on the results of the clinical examination alone, the decision to alter patient management was made in 4 of 71 visits (6%), and based on standard FA, in additional 3 of 71 visits (4%). The addition of

UWF-FA (ultra-wide-field fluorescein angiography) altered patient management in 36 of 71 visits (51%) [14].

In clinical practice, the area of the posterior pole is more commonly evaluated than the peripheral retina. Furthermore, most research is devoted to the study of different diagnostic methods for macular and optic nerve diseases. At present, optical coherence tomography (OCT) and OCT-based angiography (OCTA) have become the standard modalities in the assessment of these conditions. As for now, though, these methods are not suitable for the examination of the peripheral retina [4].

The aim of the study is to discuss the benefits of peripheral retinal angiography in clinical practice. Based on their own experience with using equipment dedicated to peripheral retinal angiography and the available literature, the authors describe the practical applications of this examination tech-

nique in patients with a range of conditions including diabetic retinopathy [6, 9, 12, 15–17], central or branch retinal artery occlusion [9, 12, 15, 18], occlusion of peripheral vessels and abnormalities due to disorders including Susac's syndrome [15, 19, 20], retinitis and chorioretinitis [9, 12, 14, 15, 21, 22], white dot syndromes [23], peripheral choroidal tumors and nevi [9, 15, 24], peripheral serous retinal detachment [15, 25] and vascular malformations such as macroaneurysms [26], Coats' disease [12] and Eales' disease.

In addition, while performing angiographic evaluation in patients with macular diseases or the indications listed above, many other changes in the peripheral retina, beyond the standard indications for FA, have also been reported, including peripheral retinal degeneration as well as retinal separation, tearing and detachment [9, 12, 15].

## DIABETIC RETINOPATHY

Diabetes mellitus is a disease in which FA is considered to be of great diagnostic value. Based on FA findings, the presence and severity of diabetic retinopathy (DR) is determined, a decision is made to initiate treatment by laser photocoagulation (LPC) of the retina, and retinal areas are selected for LPC procedures [6, 16].

In the early period, DR presents with microaneurysms, petechiae, and hard exudates, most typically located in the region of the posterior pole. The foveal avascular zone (FAZ) also increases. The development of macular edema (focal, cystic or diffuse) of varying severity is observed, producing an image consistent with diabetic macular edema (DME). Preproliferative DR is evidenced by the presence of soft exudates, intraretinal microvascular abnormalities (IRMA), arteriovenous anastomoses ("short circuits"), phleboopathy, and above all the development of avascular zones, i.e. areas without capillary perfusion. Proliferative DR is accompanied by retinal neovascularization of the disc (NVD) and neovascularization elsewhere (NVE), intravitreal hemorrhages, and preretinal effusions [12, 18].

Wide-field fluorescein angiography (WF-FA) and UWF-FA are regarded as key examinations for detecting peripheral retinal areas lacking capillary perfusion. This capability is most important in patients with type 1 diabetes, where the initial changes develop in the peripheral retina, while the macula may not show any pathological features for a prolonged period. In such cases, detecting ischemia on the periphery of the retina by FA supports the decision to refer the patient for LPC treatment, and also identifies specific areas where it should be applied. It has been found that UWF-FA performed in patients with DR reveals a substantial number of other retinal vascular pathologies. Wessel *et al.* found that ultra-wide-field imaging visualized 3.2 times more total retinal surface area than 7SF. Also, when compared with 7SF, ultra-wide-field imaging showed 3.9 times more avascular areas, 1.9 times more retinal neovascularization, and 3.8 times more areas after laser panphotocoagulation [27]. The diagnosis and monitoring of DR by applying this method may change the evaluation of DR sta-

ge and, as a result, improve disease control and treatment [27]. The emergence of changes in the far periphery may herald the progression of diabetic retinopathy and exacerbation of vascular pathologies [28]. Also, peripheral retinal ischemia was shown to correlate with the development of DME. In this case, the risk of macular edema increases 3.75 times [29].

DR represents retinal response to chronic circulatory disorders and tissue hypoxia manifesting as, among others, the presence of ischemic areas. OCTA can also be used to visualize them, but at present the examination is only used for imaging the macular area [4].

It is worth adding that FA is essential in confirming the presence and evaluating the activity of vascular proliferations (by visualizing pathological vessel leakage) when fibrous proliferations are detected clinically. It is also the only examination that shows leakage through own vessels, which is indicative of vascular wall damage (Figure 2).

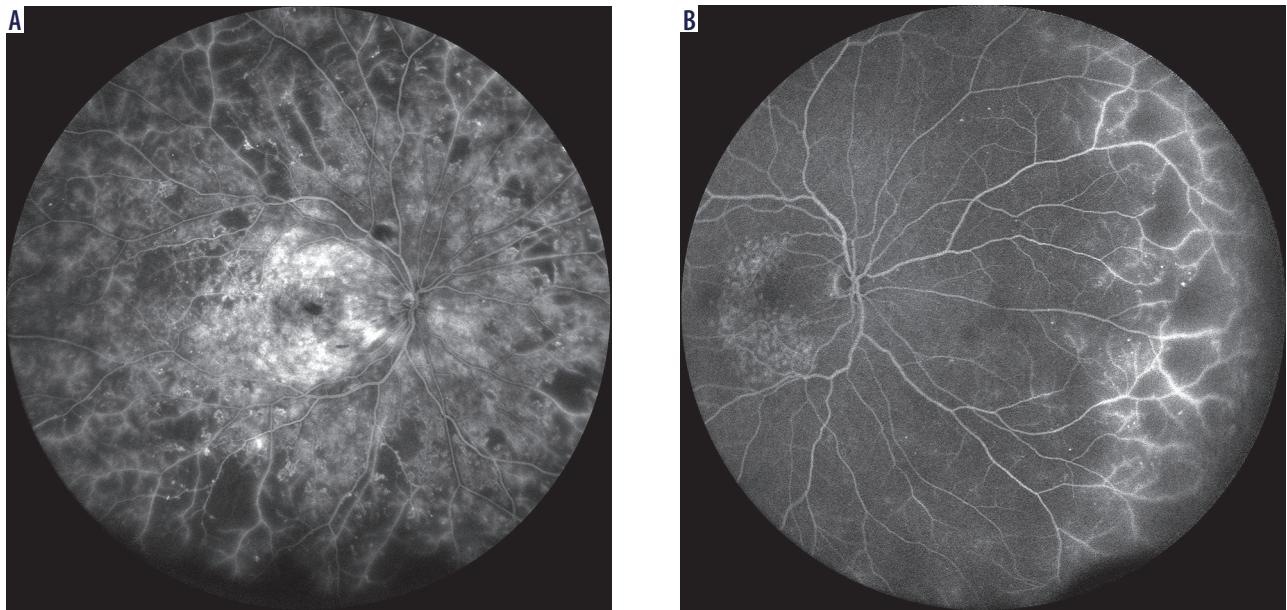
## RETINAL VEIN OCCLUSION

A crucial aspect in the diagnostic work-up of central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO) is determining the occlusion site, with or without ischemia. Ischemia is evidenced by the presence of areas without capillary perfusion. Their detection guides the decisions on further patient management.

The FA-based diagnostic process in cases of retinal vein occlusion evaluates the presence and extent of avascular zones, presence and activity of vascular proliferations, venous-venous anastomoses, as well as the occlusion site, and vascular perfusion (rate of vessel filling and emptying). On that basis, it is possible to determine the degree of vascular damage, assess patient eligibility for therapy, for example by LPC, and assess the efficacy of treatment.

Even though the majority of CRVO/BRVO lesions are located in the posterior pole, an evaluation of retinal periphery, and especially the presence of peripheral avascular zones, often with vascular amputations, is crucial for appropriate initiation of effective management [9, 18] (Figure 3). With the introduction of UWF systems, it is possible to perform LPC by selectively targeting only ischemic areas, which should be sufficient to reduce the production of vascular endothelial growth factor (VEGF) [8].

To evaluate the extent of ischemic areas, a method based on the ischemic index (ISI) was introduced. ISI is the ratio of the ischemic area to the total retinal area, and can be calculated by dedicated software in the Optos system. Based on this index, the degree of non-perfusion is established. In eyes with BRVO, the ischemic index can range from 0.1% to 61.3%, and in eyes with CRVO, from 0% to 99%. As reported by Tan *et al.*, the ISI in eyes with neovascularization is greater than 45%, while the risk of DME increases when the ISI exceeds 10%. The higher the ISI, the greater the risk of complications including retinal neovascularization, abnormalities in the filtration angle, and DME [8].



**Figure 2.** WF-FA 102° (Spectralis). Diabetic retinopathy. **A)** Extensive peripheral avascular zones, edema maculopathy. **B)** Diabetic retinopathy, after FL (grid) about 15 years ago. Full visual acuity. Peripheral, extensive avascular zones and exudative leakages. Laser photocoagulation needed

### RETINAL ARTERY OCCLUSION

In cases of clinically diagnosed central retinal artery occlusion (CRAO) or branch retinal artery occlusion (BRAO), it is important to visualize the site of vascular occlusion, establish the extent of ischemia, assess vascular perfusion, and locate transvascular leakage by FA. In BRAO, the time and rate of dye filling in an occluded vessel can be precisely tracked and compared to a normally filling vessel branch (Figure 4A).

Recent reports suggest that there are certain regularities in FA images in patients with CRAO. Based on FA findings, Gong *et al.* distinguished three types of manifestations: poor perfusion (arm-to-retina circulation time > 23 s), exudation (normal arm-to-retina circulation time but clear vascular leakage), and mixed type combining the features of the other two types [30].

Wide-angle ICGA may be useful in identifying cases of arterial occlusion due to inflammatory etiology, e.g. when giant cell arteritis (GCA) is suspected. GCA may coexist with choroidal hyperperfusion [31].

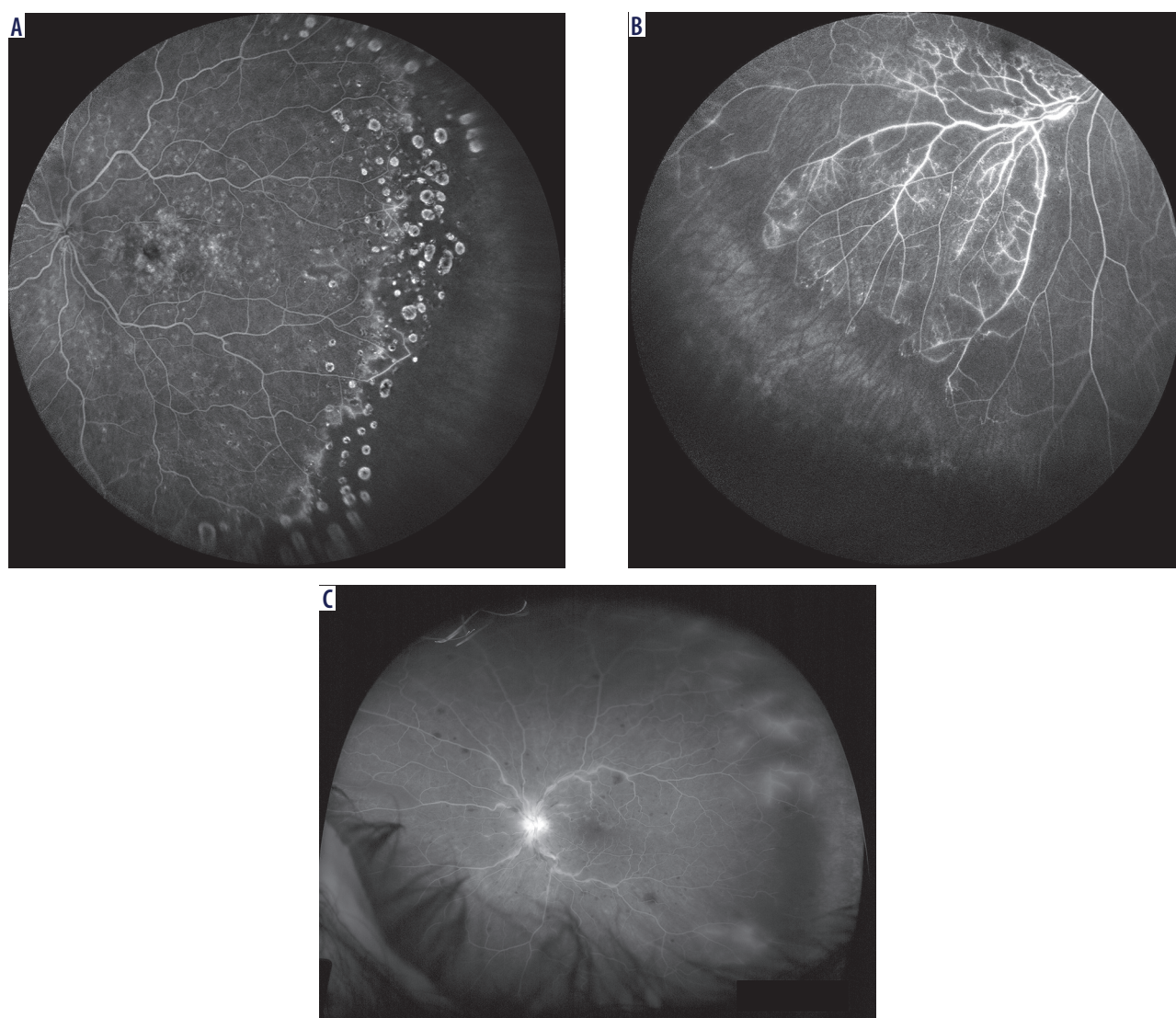
UWF-FA is of particular importance in the diagnosis and monitoring of therapy in patients with Susac's syndrome (SS). The most common manifestations are CNS changes associated with encephalopathy (damage to the small cerebral precapillary vessels) and hearing symptoms due to damage to the cochlear arterioles in the inner ear. Ocular manifestations are rare, as they affect mainly small vessels in the retinal periphery. Visualizing features typical of SS in the retina is a necessary criterion for the diagnosis of fully symptomatic syndrome [19, 32]. The authors' own observations show that abnormalities commonly encountered in SS are often not identifiable on clinical examination, and typically located in the extreme periphery of the retina. UWF-FA is a modality that clearly visualizes the characteristic features of this condition including the occlusion of large arteries

(rarely) and their peripheral branches (most commonly) by the accumulation of immune complexes, vascular amputations with peripheral avascular zones (devoid of capillary circulation) and leaks through damaged arterial vessels (often located in the extreme periphery of the retina). UWF-FA may reveal hyperfluorescence of the arteriolar walls in proximal locations to the sites of vessel occlusion (Gass plaques), and arterio-arterial anastomoses most frequently seen adjacent to peripheral ischemic areas. In the posterior pole, in addition to vascular changes, dye leakage on the optic nerve disc or optic nerve atrophy [20] can be visualized (Figure 4B, C).

### RETINITIS AND CHORIORETINITIS

Retinitis and chorioretinitis present with diverse clinical features. Systemic inflammatory diseases of various etiologies (immune, infectious or idiopathic) can also affect the ocular blood vessels. It is not uncommon for the early symptoms of systemic disorders to appear in the retinal and/or choroidal vessels. A literature review shows that wide-angle fundus images are a good screening method in inflammatory diseases of the retina and choroid [33], while UWF-FA and UWF-ICGA (ultra-wide-field indocyanine green angiography) can provide important additional insights in the treatment of retinal vasculitis [14].

The inflammatory process involving the retinal and choroidal vessels is characterized by vascular leakage, vascular occlusion, retinal edema, and the presence of inflammatory foci [14, 21, 22]. In many cases, these abnormalities are invisible in the region of the posterior pole and sometimes impossible to visualize with ophthalmoscopy. UWF-A (ultra-wide-field angiography) is the only modality that enables the detection of such changes before the macula is



**Figure 3.** WF-FA 102° (Spectralis). **A)** Non-ischemic CRVO after FL, macular edema, extensively avascular zones in the peripheral retina with vessels amputations. **B)** BRVO with peripheral ischemia, extensive avascular zones and vessels amputations in the peripheral retina and capillary leakages. **C)** UWF-FA 200° (Optos Tx200). Non-ischemic CRVO. Capillary leakages in the peripheral retina

affected (Figure 5A, B). When retinal vessels are damaged and the inner blood–retinal barrier breaks down, FA shows dye leakage, which precisely identifies areas involved in the inflammatory process. The severity of vascular leakage is correlated with the activity of inflammatory lesions. The authors' own experience shows that patients with peripheral retinal vascular leakage require ongoing monitoring, as in some cases, over time, they develop symptoms of a systemic disease of inflammatory or autoimmune etiology. Angiography also provides a possibility to visualize post-inflammatory lesions that no longer show any activity in the form of dye leakage (Figure 5C).

The periphery of the retina is a relatively common site for focal inflammatory lesions secondary to white dot syndromes, especially associated with acute posterior multifocal placoid pigment epitheliopathy (APMPPE). Indocyanine green angiography of the peripheral retina is a modality that

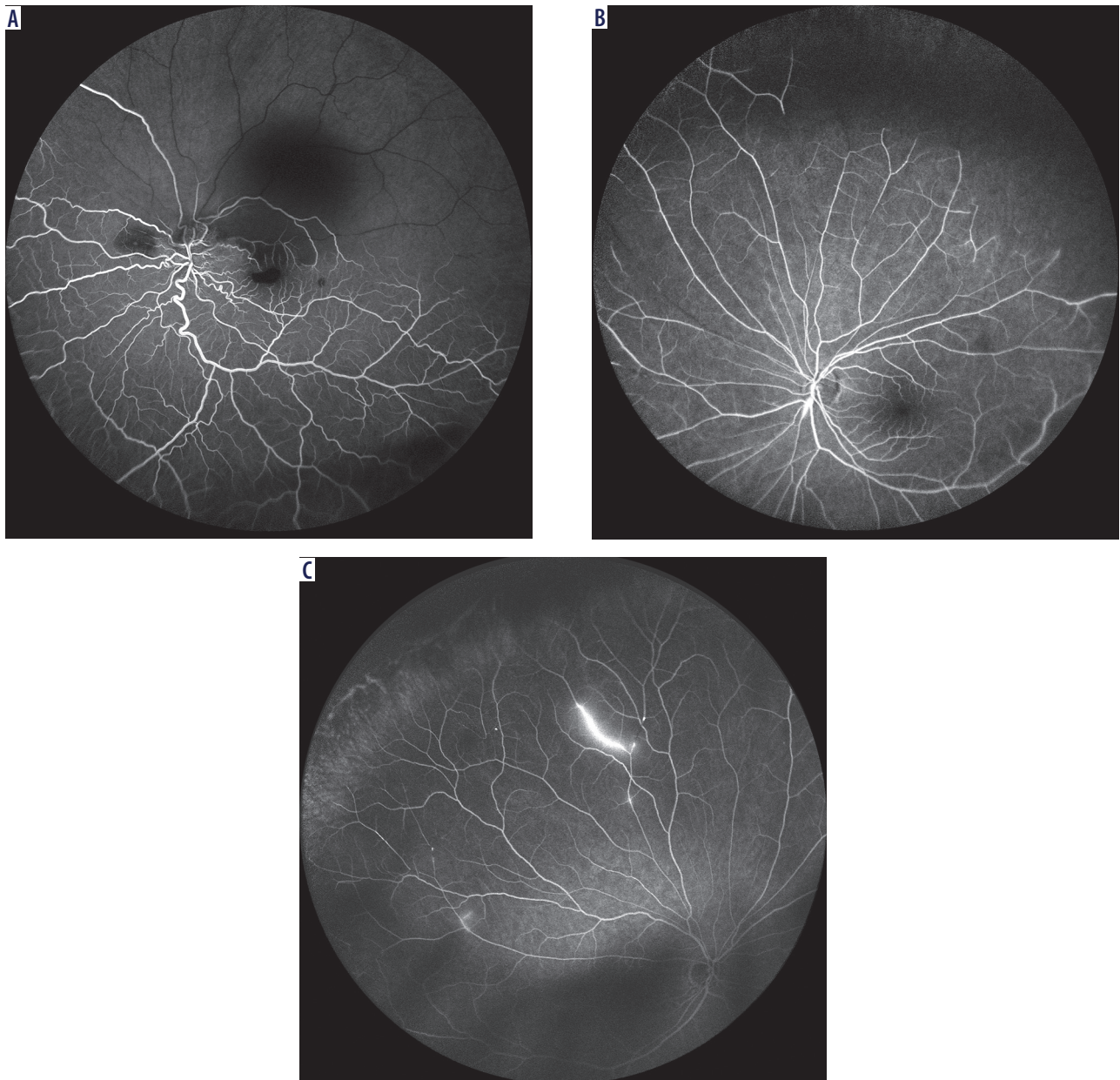
best visualizes changes that are difficult to identify by ophthalmoscopy and FA (Figure 5D).

FA evaluation of the retinal periphery is very useful in the early diagnosis of acute retinal necrosis, since early pathological changes are frequently located within the periphery and from there progress towards the posterior pole (Figure 6).

Retinitis can also present as serous peripheral retinal detachment, which is clearly visible on UWF-FA images. The technique is also suitable for the assessment of progression of changes (Figure 7).

### TUMORS AND NEVI

In addition to ophthalmoscopy, color fundus photography and ultrasound evaluation, other modalities that can be used in daily clinical practice to determine the size, shape and other important features of suspicious changes observed in the fundus are angiographic examinations (FA



**Figure 4.** WF-FA 102° (Spectralis). **A)** BRAO (upper temporal) with delayed vascular bed filling. **B)** Susac syndrome. Peripheral vascular amputations with retinal ischemia. Segmental lack of dye flow in some arterial vessels. **C)** Susac syndrome. Peripheral leakages through arterial vessels. Gass plaques

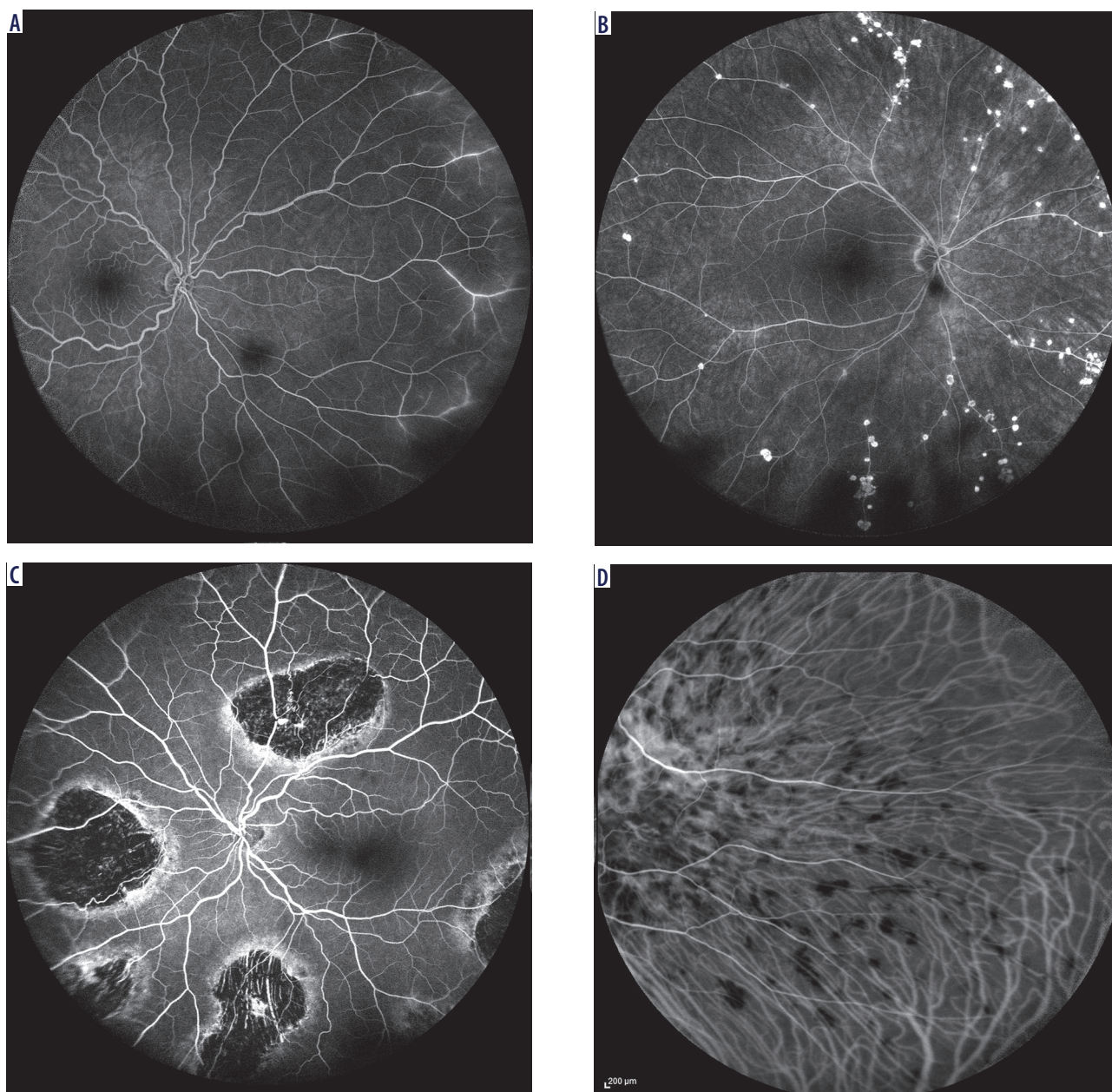
and ICGA). Such changes may be benign (e.g. nevi, RPE hyperplasia, hemangioma) or malignant (e.g. metastasis or melanoma). Wide-angle imaging is useful for documenting lesions located beyond the posterior pole. Angiographic examinations play a role in determining whether a lesion is benign or malignant. They show the growth of the tumor's vessels and dye leakage, which most typically suggests the malignant nature of the lesion. The severity of leakage is indicative of potential tumor activity. UWF-A visualizes the tumor site and typically also the extent of coexisting serous retinal detachment. It also reveals the presence of associated lesions such as drusen, lipofuscinosis, and petechiae. UWF-FA is indispensable for detecting the presence of avascular areas secondary to radiation retinopathy following brachy-

therapy, which may require treatment by laser photocoagulation (Figure 8).

#### OTHER PERIPHERAL RETINAL PATHOLOGIES

Angiography is most commonly performed in the diagnostic work-up of changes located in the posterior pole such as age-related macular degeneration (AMD), central serous chorioretinopathy (CSCR), macular neovascularization (due to myopia, Best's disease, choroidal rupture, idiopathic type), as well as maculopathy of various origins.

The authors' own experience shows that additional angiograms of the peripheral retina yield benefits in the angiographic diagnostics of macular disorders, as they are capable of visualizing changes that often require further diagnostic



**Figure 5.** WF-FA 102° (Spectralis). **A)** Subclinical vasculitis. Peripheral capillary leakages. **B)** Diffuse, peripheral retinitis, posterior pole unchanged. **C)** Peripheral inflammation scars with atrophy, posterior pole unchanged. **D)** ICGA 55° (Spectralis). Acute posterior multifocal placoid pigment epitheliopathy (APMPPE). Peripheral inflammation of the choroid and subtle changes in the slit lamp exam and FA

and therapeutic management. They include choroidal and retinal detachment, peripheral vascular malformations, mild peripheral retinal degenerations (e.g. honeycomb type), retinal tears requiring treatment by laser photocoagulation, tears, holes, and degenerative changes managed by LPC (Figure 9).

## DISCUSSION

The imaging of pathologies located in the fundus of the eye has played an important role in ophthalmology for a long time, contributing to the diagnosis, monitoring and assessment of patient eligibility for treatment. The value of angiographic examinations is best evidenced by the fact that,

despite the passage of time and incorporation of new examination types into clinical practice, angiography continues to be a regular element in the arsenal of diagnostic options. However, the introduction of OCT and OCTA examinations which are non-invasive and quick to perform has changed to some extent the list of indications for FA and ICGA. Still, angiographic examinations will retain their status as the most important modality for the assessment of retinal changes occurring in diabetic retinopathy, CRVO or BRVO, retinal arterial occlusion due to Susac's syndrome, vascular malformations, and all inflammatory conditions affecting the retinal and choroidal vessels.



Technological advances – mainly the introduction of laser techniques – have made it possible to visualize the far periphery of the retina in FA and ICGA as well. With modern angiography systems, it is possible to perform imaging examinations of the peripheral retina without pupil dilation and despite reduced clarity of the optical media, which is a benefit for patients. Another advantage of currently used angiography systems is the application of digital image processing technology.

Recent reports have clarified the field-of-view terminology for imaging changes in the fundus on the basis of visible anatomical structures. When visualizing the posterior eye segment, a photograph of the entire retina (360°), up to the ora serrata, is an advisable option, though there is as yet no clinically available technology to obtain a single image capturing such a wide field of view.

Nagiel *et al.* argue that peripheral retinal angiography should be currently recognized as the standard retinal examination [15]. Ultra-wide-angle imaging has already become an indispensable tool for the assessment of peripheral retinal pathology, and it may also become a foundation for screening and telemedicine. Observations made by the authors of this study are consistent with the above conclusions. However, it needs to be noted that these systems are very expensive and it is difficult to imagine that they might find their way into widespread application. Wide-angle imaging may contribute to the diagnostic and therapeutic management in multiple retinal vascular disorders by supplying clinicians with additional information. Photographs of the peripheral retina may be taken during routine angiography.

A point to be made is that retinal vasculature consists of the only vessels of such caliber in the human body that can be visualized in living persons, so their assessment may indirectly reveal the condition of the vessels in other body organs. Retinitis and chorioretinitis may be the first signs of the onset of a systemic pathology. Early detection of systemic diseases makes it possible to initiate appropriate treatment. In addition, the severity of retinal vascular leakage can be indicative of the activity of the systemic inflammatory process, enabling the cli-

nician to prescribe a new or modify existing treatment, as highlighted by Laovirojjanakul *et al.* The same authors point out that in cases of pars planitis UWF-FA may reveal changes that are not visible on ophthalmoscopic examination [22].

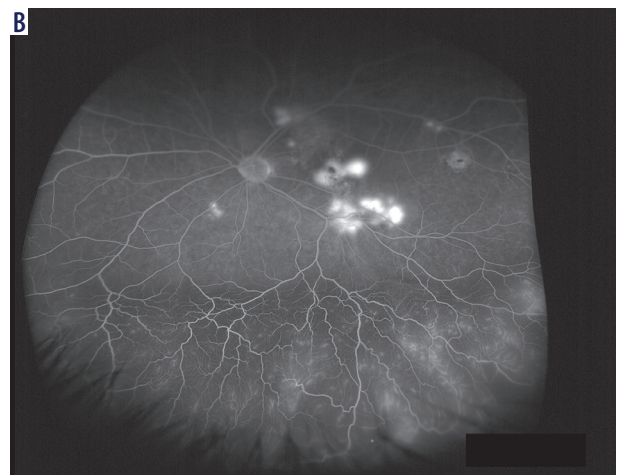
Ischemic peripheral retinal areas secondary to vascular diseases require appropriate management (e.g. LPC, cryoapplication), while accurate diagnosis can be achieved by performing angiographic evaluation of the retinal periphery, as indicated by Rabiolo *et al.* (in DR) [16] and Spaide (in CRVO) [18].

## CONCLUSIONS

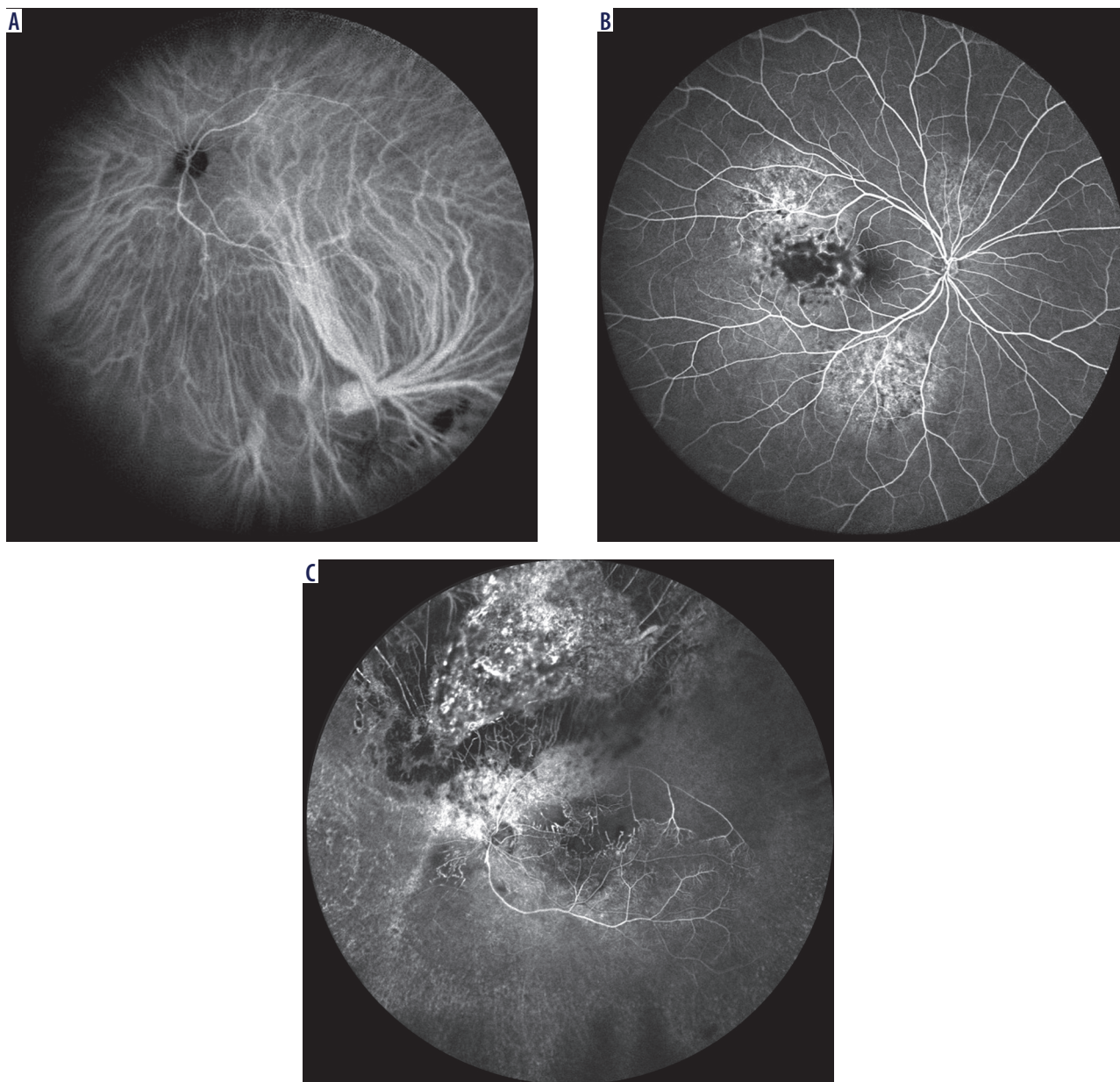
Wide-angle imaging of the posterior segment of the eye has the greatest value in patients with vascular diseases involving the periphery of the retina, including diabetic reti-



**Figure 6.** WF-FA 102° (Spectralis). Acute retinal necrosis. Unobstructed posterior pole capillaries with leakages. Peripheral capillaries with necrosis



**Figure 7.** UWF-FA 200° (Optos 200Tx). Serum retinal detachment, peripheral, temporal and lower part of the fundus. **A)** Right eye. **B)** Left eye (the same patient), capillary leakages in the macula



**Figure 8.** **A)** WF-ICGA 102° (Spectralis). Choroid nevus located peripheral and at the bottom of the fundus. **B)** WF-FA 102° (Spectralis). Breast cancer metastases to choroid (after chemotherapy). Lesions located temporally from the macula, above the optic nerve disc and below the lower temporal arches. **C)** Radiation retinopathy, after brachytherapy of melanoma located in the upper part of the fundus. Own capillaries located only in the posterior pole, rest of the retina is a big avascular zone

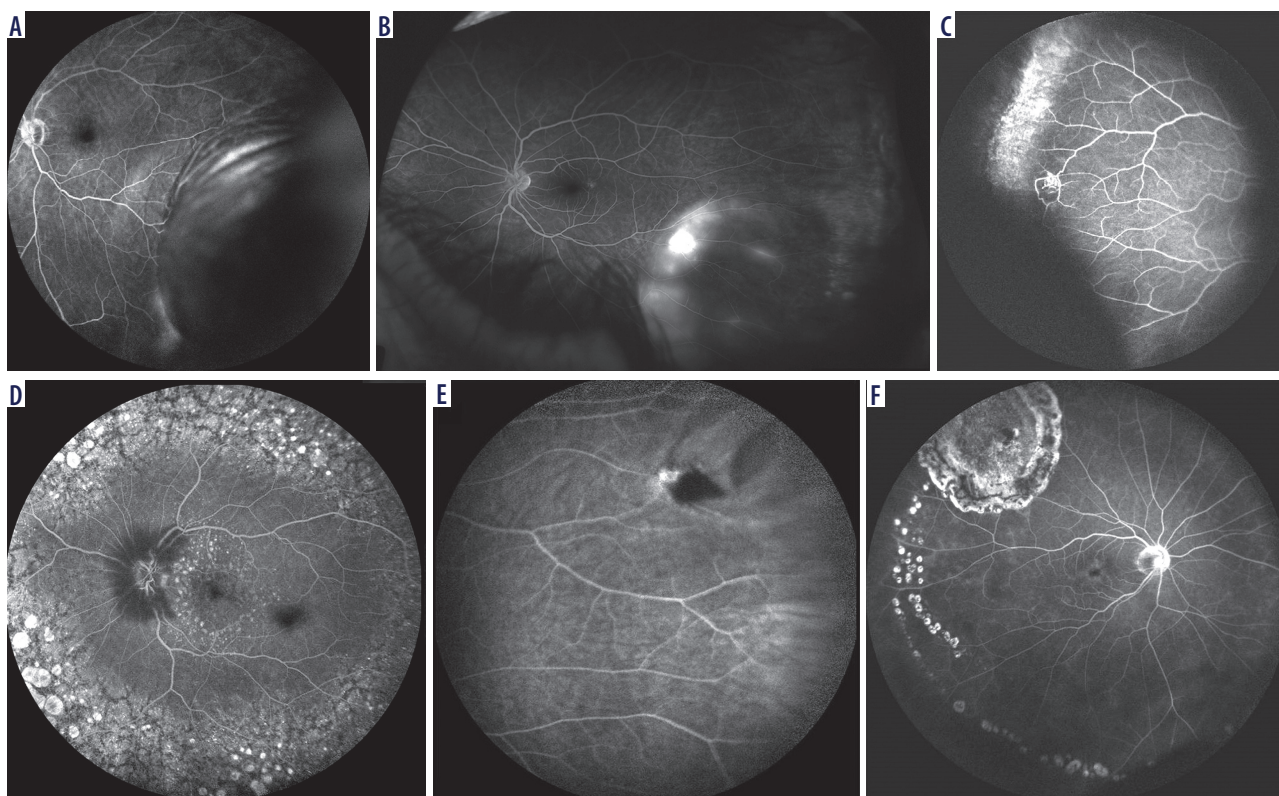
nopathy, retinal venous and arterial occlusion, Susac's syndrome, peripheral vascular malformations, and inflammatory diseases of the retina and choroid, and may contribute to the diagnostic and therapeutic management by providing clinicians with useful supplementary information.

The authors' own experience shows that additional angiograms showing the peripheral retina are justified during the angiographic diagnostic work-up of macular diseases (also with the use of standard lenses with a FoV of up to 50°), so that changes frequently requiring an extended diagnostic assessment can be visualized.

Modern angiography systems offer a possibility to perform imaging examinations of the peripheral retina without pupil dilation and despite reduced clarity of the optical media, which is beneficial for patients. However, patient compliance is required throughout the examination. The adverse effects associated with the dyes used, and the precautions that must be followed with UWF-A, are the same as in the conventional FA and ICGA modalities.

#### DISCLOSURE

The authors declare no conflict of interest.



**Figure 9.** **A)** WF-FA 102° (Spectralis). Peripheral choroidal detachment (after glaucoma surgery). **B)** UWF-FA 200° (Optos 200Tx). Retinal dissection, temporal-lower part of the fundus. **C)** WF-FA 102° (Spectralis). Peripheral vascular malformations. **D)** WF-FA 102° (Spectralis). Honeycomb retinal degeneration. **E)** FA 50° (Zeiss FF450). Peripheral retinal tear with flap requiring photocoagulation. **F)** WF-FA 102° (Spectralis). Peripheral retinal tear after laser photocoagulation

## References

1. Novotny HR, Alvis DL. A method of photographing fluorescence in circulating blood in the human retina. *Circulation* 1961; 24: 82-86.
2. Flower RW, Hochheimer BF. A clinical technique and apparatus for simultaneous angiography of the separate retinal and choroidal circulations. *Invest Ophthalmol* 1973; 12: 248-261.
3. Gawęcki M. *Angiografia fluoresceinowa i indocyjaninowa: Praktyczny podręcznik*. Gdańsk: KMG Dragon's House, 2016.
4. Turczyńska M, Krajewski P, Brydak-Godowska J, Kęćik D. *Wybrane metody nowoczesnej diagnostyki chorób siatkówki*. Medycyna po Dyplomie. Updated 2019; 2019: 38-46.
5. Turczyńska M, Kuźnik-Borkowska A, Kęćik D. *Metody obrazowania zmian degeneracyjnych plamki*. Okulistyka. Updated 2015; 1: 14-19.
6. Paćkowska M, Turczyńska M. *Rola angiografii fluoresceinowej i indocyjaninowej w diagnostyce retinopatii cukrzycowej*. Okulistyka. Updated 2007; 2: 30-32.
7. Fariza E, Ormerod LD, O'Day T, Celorio JM. Practical anterior segment fluorescein angiography. *Graefes Arch Clin Exp Ophthalmol* 1991; 229: 105-110.
8. Tan CS, Li KZ, Sadda SR. Wide-field angiography in retinal vein occlusions. *Int J Retina Vitreous* 2019; 5 (Suppl 1): 18.
9. Bajwa A, Aman R, Reddy AK. A comprehensive review of diagnostic imaging technologies to evaluate the retina and the optic disk. *Int Ophthalmol* 2015; 35: 733-755.
10. Choudhry N, Duker JS, Freund KB, et al. Classification and Guidelines for Widefield Imaging: Recommendations from the International Widefield Imaging Study Group. *Ophthalmol Retina* 2019; 3: 843-849.
11. Webb RH, Hughes GW, Delori FC. Confocal scanning laser ophthalmoscope. *Appl Opt* 1987; 26: 1492-1499.
12. Witmer MT, Kiss S. Wide-field imaging of the retina. *Surv Ophthalmol* 2013; 58: 143-154.
13. Ilginis T, Clarke J, Patel PJ. Ophthalmic imaging. *Br Med Bull* 2014; 111: 77-88.
14. Leder HA, Campbell JP, Sepah YJ, et al. Ultra-wide-field retinal imaging in the management of non-infectious retinal vasculitis. *J Ophthalmic Inflamm Infect* 2013; 3: 30.
15. Nagiel A, Lalane RA, Sadda SR, Schwartz SD. ULTRA-WIDEFIELD FUNDUS IMAGING: A Review of Clinical Applications and Future Trends. *Retina (Philadelphia, Pa.)* 2016; 36: 660-678.
16. Rabiolo A, Parravano M, Querques L, et al. Ultra-wide-field fluorescein angiography in diabetic retinopathy: a narrative review. *Clin Ophthalmol (Auckland, N.Z.)* 2017; 11: 803-807.
17. Brown DM. Advancing the Detection and Management of Diabetic Retinopathy with Ultra-widefield Retinal Imaging. *US Ophthalmic Review* 2017; 10: 23.
18. Spaide RF. Peripheral areas of nonperfusion in treated central retinal vein occlusion as imaged by wide-field fluorescein angiography. *Retina (Philadelphia, Pa.)* 2011; 31: 829-837.

19. Kęćcik T, Brydak-Godowska J, Dróbecka-Brydak E, et al. Zespół Susaca – mikroangiopatia naczyń siatkówki, ślimaka i mózgu. *Okulistyka*. Updated 2001; 4: 49-51.
20. Seifert-Held T, Langner-Wegscheider BJ, Komposch M, et al. Susac's syndrome: clinical course and epidemiology in a Central European population. *Int J Neurosci* 2017; 127: 776-780.
21. Brydak-Godowska J, Turczyńska M, Przybyś M, et al. Ocular Complications in Influenza Virus Infection. *Ocul Immunol Inflamm* 2019; 27: 545-550.
22. Laovirojjanakul W, Acharya N, Gonzales JA. Ultra-Widefield Fluorescein Angiography in Intermediate Uveitis. *Ocul Immunol Inflamm* 2019; 27: 356-361.
23. Brydak-Godowska J, Gołębiewska J, Turczyńska M, et al. Observation and Clinical Pattern in Patients with White Dot Syndromes: The Role of Color Photography in Monitoring Ocular Changes in Long-Term Observation. *Med Sci Monit* 2017; 23: 1106-1115.
24. Golebiewska J, Kęćcik D, Turczyńska M, et al. Optical coherence tomography in diagnosing, differentiating and monitoring of choroidal nevi - 1 year observational study. *Neuro Endocrinol Lett* 2013; 34: 539-542.
25. Gołębiewska J, Brydak-Godowska J, Moneta-Wielgoś J, et al. Correlation between Choroidal Neovascularization Shown by OCT Angiography and Choroidal Thickness in Patients with Chronic Central Serous Chorioretinopathy. *J Ophthalmol* 2017; 2017: 3048013.
26. Turczyńska M, Brydak-Godowska J, Kęćcik D. Obraz makrotętniaka tętnicy siatkówki w badaniu OCT. *Okulistyka*. Updated 2011; 3: 91-95.
27. Wessel MM, Aaker GD, Parlitsis G, et al. Ultra-wide-field angiography improves the detection and classification of diabetic retinopathy. *Retina (Philadelphia, Pa.)* 2012; 32: 785-791.
28. Silva PS, Dela Cruz AJ, Ledesma MG, et al. Diabetic Retinopathy Severity and Peripheral Lesions Are Associated with Nonperfusion on Ultrawide Field Angiography. *Ophthalmology* 2015; 122: 2465-2472.
29. Wessel MM, Nair N, Aaker GD, et al. Peripheral retinal ischaemia, as evaluated by ultra-widefield fluorescein angiography, is associated with diabetic macular oedema. *Br J Ophthalmol* 2012; 96: 694-698.
30. Gong H, Song Q, Wang L. Manifestations of central retinal artery occlusion revealed by fundus fluorescein angiography are associated with the degree of visual loss. *Exp Ther Med* 2016; 11: 2420-2424.
31. Tang PH, Lee MS, van Kuijk FJ. Ultra Wide-Field Indocyanine Green Angiogram Highlights Choroidal Perfusion Delay Secondary to Giant Cell Arteritis. *Ophthalmic Surg Lasers Imaging Retina* 2016; 47: 471-473.
32. Bóle głowy: Przypadki kliniczne. 1<sup>st</sup> ed. Medical Education, Warszawa 2019.
33. Cheng SCK, Yap MKH, Goldschmidt E, et al. Use of the Optomap with lid retraction and its sensitivity and specificity. *Clinical and Experimental Optometry* 2008; 91: 373-378.