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# Ultra-widefield angiography in the diagnosis and management of uveitis

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## Abstract:

**PURPOSE:** The aim of this study is to evaluate the clinical use of ultra-widefield angiography (UWFA) in uveitis.

**MATERIALS AND METHODS:** We showed the UWFA and traditional 55° fluorescein angiography (FA) of four cases with Eales' disease, idiopathic retinal vasculitis, aneurysms, and neuroretinitis syndrome, Behçet's disease, and idiopathic panuveitis in a tertiary medical center. Comparison of UWFA with traditional 55°FA in the diagnosis and management of uveitis and review of the literature is also presented.

**RESULTS:** Ultra-widefield FA revealed far-peripheral vascular imaging. This information would not have been easily obtained from traditional FA. With more information of the peripheral retina, it may facilitate appropriate diagnosis and monitoring, and the management may be revised.

**CONCLUSION:** University of Western Australia played an important role to confirm the diagnosis of uveitis and to determine the corresponding treatment.

## Keywords:

Eales' disease, idiopathic retinal vasculitis, aneurysms, and neuroretinitis, intraocular tuberculosis, ultra-widefield fluorescein angiography, ultra-widefield indocyanine green angiography

## Introduction

Fluorescein angiography (FA) and indocyanine green angiography (ICGA) are vital examinations in the evaluation of uveitis. Traditional angiography takes images of central retina 30°–55°. The peripheral retina image is hard to obtain, and the quality is degraded due to the eye's optical aberrations. To overcome the limitations, 7- or 9-field montage FA images are commonly used to demonstrate the findings of peripheral retina and can extend up to 96° under ideal circumstances.<sup>[1-3]</sup> However, montage FA images require highly skilled technicians, cooperative patients, and could not get simultaneous images of the posterior pole and the periphery.<sup>[4,5]</sup>

Ultra-widefield (UWF) imaging is the imaging angles larger than the standard reference 30° and the widefield 55°.<sup>[6,7]</sup> Several contact imaging systems have been developed for providing wider field retina image. These include the Pomerantz camera, the Retcam (Clarity Medical Systems, Inc., Pleasanton, CA, USA), the Panoret-1000™ camera (Medibell Medical Vision Technologies, Haifa, Israel), and the Staurenghi lens (Ocular Staurenghi 230 scanning laser ophthalmoscope (SLO) Retina Lens; Ocular Instruments Inc., Bellevue, WA, USA), allowing imaging up to the 100°–160° but with limited resolution.<sup>[8-11]</sup>

With the introduction of the confocal SLO, UWF angiography (UWFA) has obtained the more distinct images of peripheral retina previously unavailable and moreover in a single shot. One of the most widely used UWF systems is the Optos®

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noncontact camera (Optos PLC, Dunfermline, UK). The Optos® system utilizes an ellipsoid mirror to produce approximately 200 internal degrees of view. Later, a noncontact UWFA module for the Spectralis® and Heidelberg retina angiograph (HRA2) has been developed. The Heidelberg Spectralis UWFA imaging system (Heidelberg Engineering, Heidelberg, Germany) provides 105°, high-contrast, and undistorted peripheral retinal image. Both UWFFA and (UWF ICGA) could be gained individually or simultaneously.<sup>[12,13]</sup>

Uveitis can develop in all parts of an eye and may include unclear pathophysiologies. Especially, in those who had poorly understood etiology or complicated conditions, appropriate diagnosis requires careful ocular examination and illumination of the clinical symptoms and signs. Many essential diagnostic clues are identified with FA; however, these signs are sometimes peripheral and difficult to be seen with traditional angiography. Consider that peripheral retinal vasculitis might be affected in many types of uveitis and related with the severity of the disease, several reports have demonstrated potential roles of the UWF imaging in the management of posterior segment disease and even anterior uveitis.<sup>[14-20]</sup> Hence, detecting peripheral vascular abnormalities is essential to diagnose, record the process, and observe the response to the treatment.

The purpose of this article focuses on UWFFA and UWF ICGA in the diagnosis and management of uveitis with peripheral retinal involvement. Comparison of UWFFA and UWF ICGA with traditional 55° FA images in cases of Eales' disease, idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN), Behçet's disease, and idiopathic panuveitis are presented, and the literature is also reviewed.

### Clinical utility in the uveitis and photo presentation

Eales' disease is characterized by overlapping stages of venous inflammation, occlusion, and retinal neovascularization (NV), especially at periphery. Diagnosis is mostly clinical retinal finding and requires exclusion of other systemic or ocular conditions.<sup>[21]</sup>

Traditional 55° FA in a case of Stage III b Eales' disease only showed vascular tortuosity, peripheral retinal NV, and macular edema OS. There was no remarkable finding in traditional 55° FA OD [Figure 1, central circle]; however, the Heidelberg Spectralis UWFFA and UWF ICGA showed peripheral retinitis and vasculitis [Figure 1]. Therefore, further treatment and close monitoring of both eyes were still necessary.

IRVAN syndrome is a rare clinical entity of unknown etiology with the striking features including retinal vasculitis, aneurysms, and neuroretinitis.

Traditional 55° FA in a case of IRVAN only showed retinal hemorrhage without obvious capillary nonperfusion OS [Figure 2, central circle]; however, the Heidelberg Spectralis UWFA showed widespread peripheral vasculitis and multiple peripheral background hypofluorescence area corresponding to capillary nonperfusion and retinal NV [Figure 2]. Thus, panretinal laser photocoagulation was performed for the capillary nonperfusion area, and cyclosporine 100 mg was prescribed once daily to control the disease activity.

Behçet's disease is a rare vasculitic disorder that is characterized by a triple-symptom complex of recurrent oral aphthous ulcers, genital ulcers, and uveitis. In a case of Behçet's disease, traditional 55° FA only showed focal retinal arteriole occlusion and retinal hemorrhage OD [Figure 3, central circle]; however, the Heidelberg Spectralis UWFFA and UWF ICGA [Figure 3] showed widespread retinal vascular leakage. Therefore, close monitoring and aggressive treatment of both eyes were still necessary.

Idiopathic panuveitis is a rare inflammatory ocular disease of unknown etiology, characterized by generalized inflammation of the uvea, retina, and vitreous. In a case of idiopathic panuveitis, traditional 55° FA [Figure 4, central circle] only showed focal retinal vascular leakage and retinal hemorrhage OD; however, the Optos® noncontact camera showed peripheral multifocal retinal lesions [Figure 4] which alerted physicians to pay attention.

## Discussion

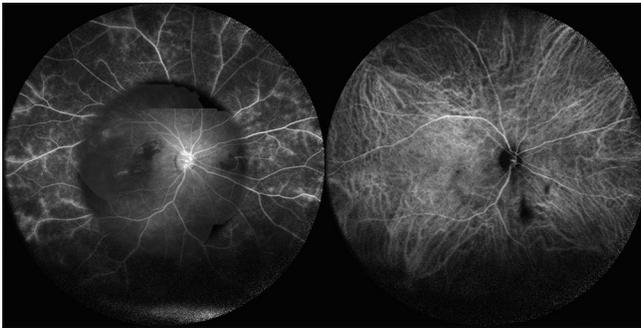
Singer *et al.* have published a prospective, observational study, and it showed the mean radial surface distance from the center of the optic disc to the peripheral edge of the visible vasculature in normal eyes was  $20.3 \pm 1.4$  mm and the mean area of the normal perfused retina was  $977.0 \text{ mm}^2$ .<sup>[22]</sup> The distances to the perfused vascular border were shorter in older individuals ( $\geq 60$  years) than



**Figure 1:** There was no remarkable finding in traditional 55° fluorescein angiography oculus dextrus (central montage image); however, the Heidelberg Spectralis ultra-widefield fluorescein angiography and ultra-widefield indocyanine green angiography showed peripheral retinitis and vasculitis



**Figure 2:** Traditional 55° fluorescein angiography showed retinal hemorrhage without obvious capillary nonperfusion oculus sinister (central montage image); however, the Heidelberg Spectralis ultra-widefield angiography showed widespread peripheral vasculitis and multiple peripheral background hypofluorescence area corresponding to capillary nonperfusion and retinal NV



**Figure 3:** Traditional 55° fluorescein angiography showed focal retinal arteriole occlusion and retinal hemorrhage oculus dextrus (central montage image); however, the Heidelberg Spectralis ultra-widefield fluorescein angiography and ultra-widefield indocyanine green angiography showed widespread retinal vascular leakage



**Figure 4:** Traditional 55° fluorescein angiography showed focal retinal vascular leakage and retinal hemorrhage oculus dextrus (central montage image); however, the Optos® noncontact camera showed peripheral multifocal retinal lesions

in younger individuals.<sup>[22]</sup> The Optos claims to image 200 internal degrees of retina, approximately 82% of the

total retinal surface area. UWFFA still has its limitation of incapable of imaging ora to ora.

Uveitis is a potential sight-threatening inflammatory eye condition that may involve the retinal vessels. Retinal vasculitis is an important entity of posterior uveitis which is generally defined as a retinal vascular nonperfusion, retinal hemorrhages, vascular sheathing, overlying vitritis, and with leakage on fluorescein in the sense of clinical vessel wall changes seen by ophthalmoscopy and/or fundus FA.<sup>[23]</sup>

As the site of substantial and possible pathology, visualization of the peripheral retina has become essential to the screening, diagnosis, management, and follow-up of many eye diseases. The benefits of the UWF imaging system have been shown in various retinal disease, including diabetes,<sup>[5,24-26]</sup> retinal vein occlusions,<sup>[27]</sup> choroidal masses,<sup>[28,29]</sup> uveitis,<sup>[4,14-20]</sup> retinal vasculitis,<sup>[30]</sup> choroidal dystrophy,<sup>[31]</sup> retinal detachment,<sup>[32]</sup> and retinopathy of prematurity.<sup>[8,33]</sup> In a current study, 42% of the patients with a diagnosis of anterior uveitis were found to have additionally peripheral vessel leakage by UWFFA.<sup>[20]</sup> This could bring doubt about the diagnosis of anterior uveitis.

UWFFA revealed far-peripheral vascular pathology and aided in treatment and monitoring. This information would not have been obtained from traditional FA. With more information of the peripheral retina, the management may be revised. As previous studies, it was shown that the management in 48% and 51% of their noninfectious uveitis study population were changed based on the UWFFA.<sup>[17,18]</sup> Peripheral vessel leakages may observe in the patients with clinically quiescent condition, which suggests possible incomplete resolution of the inflammation and change the treatment strategy.

The image quality and utility of montage FA, Optos® Optomap®, and Heidelberg Spectralis® were compared in several studies. Except less degrees of peripheral retina visualization, montage FA could not get the same phase of central and peripheral retina simultaneously. One of this drawbacks is leakage in the late phase would obscure the details of the leaking sites. When compared Optos® Optomap® with Heidelberg Spectralis®, the presence of lid and lash artifacts that were noticed more often in the Optos® Optomap® images.

The ultra-widefield Heidelberg Spectralis module can image more peripherally at the superior and inferior retina than the Optos, whereas the Optos is more effective in the temporal and nasal area and have a larger total retinal area image. Although Optos® Optomap® imaged a larger total retinal surface area, it appears distorted, especially in the far temporal and nasal periphery, due to

its utilization of an ellipsoid mirror to image the retina.<sup>[13]</sup> On the other hand, undistorted and clear flat images of the central and peripheral retina could be obtained by the Heidelberg Spectralis® HRA2 noncontact lens in a single image. In spite of the improvement of imaging technology, peripheral retinal examinations with scleral indentation by the binocular indirect ophthalmoscopy are still mandatory.

In all four patients demonstrated, UWFFA revealed far-peripheral vascular pathology which traditional 55° FA did not disclose. UWFFA facilitated appropriate treatment and monitoring. This information would not have been obtained from traditional 55° FA. By providing more information of the peripheral retina than traditional FA is able to, UWFFA directly led to the revision of clinical management.

## Conclusion

UWFFA imaging will play an essential role in the clinical evaluation and management in the uveitis in the future. Image studies of peripheral retinal lesions help us to understand more about the pathophysiology and the process of uveitis. Larger, prospective studies and inclusion of different types of uveitis are still necessary to evaluate more completely the clinical utility of UWFFA.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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