Expanding the View in the Posterior Segment

Ultra-widefield retinal imaging is helping to transform the identification and management of retinal disease.

By Szilárd Kiss, MD

It is a simple truth in the vitreoretinal subspecialty that it is more difficult to diagnose or manage something that we have trouble seeing. It has also become evident that the regions of the retina that have been the most difficult to visualize are often the site of early and important signs of an active disease process.1 We simply cannot afford to miss the periphery any longer. Fortunately, the availability of single-capture, ultra-widefield (UWF) retinal imaging technology is facilitating unprecedented visual inspection of the peripheral retina and is beginning to change the way we identify, characterize, and manage retinal pathology. While the technology continues to advance and its full clinical utility is still being explored, there can be little doubt that UWF retinal imaging will play an increasingly important role in your practice.

The Evolution of UWF Imaging

The first fundus camera, providing a 20° field of view, became commercially available in 1926. Soon after, the capability to view a 30° image was developed and became the standard for the traditional fundus camera. Anything beyond 30° became known as widefield. The traditional fundus camera consisted of a camera attached to a low-power microscope. It required pupillary dilation and patient cooperation. Images could be combined to create a montage, the ETDRS 7-standard fields composite image (Figure 1) providing approximately a 100° view of the fundus (depending on the aperture used). In 1975, a contact lens-based device was developed that separated the camera from the light source. The light source lit the eye with fiber optic transpupillary and transscleral illumination. The result of this lighting was a 148° capture from the retina anterior to the equator.

In 1997, a device became available that used a contact lens and a fiber optic light source connected to a computer to view the peripheral retina digitally, providing a field of view up to 130°. This was particularly useful for capturing images in patients unable to position themselves, such as neonates and infants. A major limitation in this technology was its inability to capture clear images if lens opacity existed. Shortly thereafter, an imaging system was developed that captured a 100° view of the retina that did not require pupillary dilation. It utilized a contact lens, transscleral illumination, and digital imaging. The advantage of this system was its use in patients with small pupils, cataracts, or intraocular lens implants.

What we now call UWF imaging emerged in 2000, when Optos combined a scanning laser ophthalmoscope with an ellipsoidal mirror providing two focal points, including a virtual focal point located posterior to the iris plane, to provide noncontact imaging of the retinal periphery with one capture. The system provides the ability to capture red and green reflectance imaging, as well as fundus autofluorescence (FAF) and fluorescein angiography (FA). This system obviated the need for dilation or contact lenses and allowed for imaging up to 200° or approximately 82% of the retina at 1 time, encompassing the central pole, midperiphery, and periphery. Since then, another system has introduced widefield imaging capabilities by combining a contact lens with a confocal scanning laser ophthalmoscope to provide a wide-angle view and, most recently, a noncontact lens module that attaches to the camera head to image the peripheral retina while permitting fluorescein and indocyanine green angiography. Among available instruments, however, the Optos systems provide the widest field of view, imaging at least 50% more of the retinal periphery than other systems (Figure 2).2
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The Optos approach

Optos overcame limitations of earlier systems by incorporating the large ellipsoidal mirror and by employing 2 lasers, green (532 nm) and red (633 nm) that facilitate visualization of retinal substructures in their individual laser separations. The green laser scans from the sensory retina to the pigment epithelium layers while the red laser scans from the pigment epithelium to the choroid. The majority of the field is captured in a single shot, rather than multiple scans that require dilation, are more time consuming, require continuous light exposure and are more burdensome on the patient. The captured digital image (the optomap) can be reviewed, evaluated, and manipulated easily. The system’s software permits adjustments to magnification, contrast and brightness to enhance areas of interest and allows measurements, annotations, clinical notes, and diagnostic tools to be added to the image. The software also facilitates sharing and reviewing by colleagues and patient education.

The most advanced UWF devices from Optos, the 200Tx, and the more compact Daytona, offer autofluorescence imaging, while the 200Tx also offers FA. FAF images are captured using the green wavelength (532 nm), which is better for visualization, particularly in the fovea, where lower wavelengths are absorbed by macular pigment, and drusen (Figures 3 and 4).

The Clinical Utility of Optos UWF Imaging

Ongoing research to explore the breadth of potential applications of Optos UWF imaging in the clinic is also confirming the value of inspecting the retinal periphery, as well as challenging the way we think about and/or approach sight-threatening diseases of the retina. Last year, Matthew Witmer, MD, and I published a major review of widefield retinal imaging in which we summarized the results of studies on a variety of available approaches, including UWF imaging, in the evaluation and management of diabetic retinopathy (DR), retinal vein occlusions, choroidal masses, uveitis, retinal vasculitis, choroidal dystrophies, retinal detachment, and pediatric retinal disease. Additional research on the use of UWF imaging, comparing imaging techniques and correlating visual findings with other diagnostic and prognostic indicators, has continued to accumulate rapidly. A brief overview of some of the most recent research shows the breadth of the potential contributions UWF is poised to make.
Optos UWF Imaging vs Standard Approaches

A basic question about UWF imaging is how this approach compares with ETDRS 7-standard field photography and the traditional dilated retinal examination. Research published in the American Journal of Ophthalmology on 206 eyes in 103 patients with type 1 or 2 diabetes and a broad distribution of DR and diabetic macular edema (DME) severity addresses this question. The authors found that exact agreement between UWF and standard photography occurred in 84% of patients, with agreement within 1 level in 91%. The nonmydriatic UWF images exactly matched clinical examination results for DR in 70% of patients and were within 1 level in 93%. The sensitivity and specificity of UWF images for detecting DR diagnosed on ETDRS photographs were 99% and 100%, respectively. The authors also noted that the UWF images were obtained more easily and rapidly, with capture taking less than half the time of ETDRS photographs even without including the time required to dilate the eyes.

Another recent study has compared Optos UWF-assisted fundus examination to traditional ophthalmoscopy in the detection of retinal pathology in 339 eyes (including patients with a history of ocular findings and patients with no known eye disease). Researchers found that the additional information provided by the optomap image helped them detect 30% more retinal lesions than the traditional dilated exam alone. When discrepancies between UWF and traditional ophthalmoscopy were adjudicated by a retinal specialist, the results revealed a statistically significant advantage for UWF in detecting a variety of pathological changes in the posterior pole/macula and the mid-to-peripheral retina.

We completed a retrospective study of 218 eyes in 145 patients to assess the utility of UWF FA in the evaluation of patients with DR, comparing the visualized retinal pathology to ETDRS 7-standard field imaging. The visualized area of the retina, retinal ischemia, retinal neovascularization, and pan-retinal photocoagulation were quantified by two independent masked graders. The respective areas identified on UWF FA were compared to a modified 7-standard field image as outlined in the ETDRS. We identified three distinct patterns of retinopathy: pathology primarily outside of the ETDRS 7-standard fields; pathology involving both posterior and peripheral retina; and pathology confined to the posterior pole. UWF FA allowed us to identify a “hotbed” of retinopathy just outside the arcades. Overall, UWF FA revealed significantly more pathology than conventional imaging in these patients with DR. Importantly, because improved visualization with UWF technology can alter the classification of DR, it may influence follow-up and treatment of these patients.

Patient Management

This potential for improved visualization with UWF technology to alter treatment approaches is being explored by other investigators, including in a pair of recently published studies. The first, an index study in 43 patients, found that Optos UWF (both color and FA) images significantly altered management decisions in noninfectious posterior uveitis compared to standard of care imaging and clinical examination. The decision to alter management was made in 33% of patients following UWF findings. UWF imaging detected uveitic changes in 12% more patients than clinical examination and conventional FA. Not only did UWF imaging produce peripheral retinal and angiographic findings not easily generated by standard methods but it also identified active disease in several patients who lacked clinical evidence of uveitis.

In a second study of 71 patients with noninfectious retinal vasculitis, the addition of Optos UWF FA altered management decisions 51% of the time, while such a change was made in only 6% with a clinical exam alone and 3% with the addition of simulated standard FA. The addition of UWF color images alone (without FA), changed the management approach 14% of the time. UWF FA also identified active disease in 68% of cases, while a clinical exam and standard FA did so in 45% of cases.

New Clinical Insights From the Periphery

The use of UWF imaging to facilitate inspection of pathology in the retinal periphery is not only providing additional information with which to make or confirm treatment decisions but is also advancing our understanding of the natural history of retinal diseases and generating related insights about improving treatment success. With the number and variety of effective interventions for sight-threatening retinal disorders, including age-related macular degeneration (AMD) and DME, continuing to expand, much of current UWF research is focused on applying observations from the periphery to the development of new therapeutic strategies (Figure 5).
A recent paper describes imaging results from patients with AMD (n=200) and no disease (n=19) using Optos UWF FAF. Overall, 69% of patients had peripheral FAF abnormalities (86% of eyes with neovascular AMD, 73% of eyes with nonneovascular AMD, and 18% of non-diseased eyes) and there was a strong correlation between these peripheral FAF patterns and the clinical features of the disease. The investigators propose a classification system for distinct patterns seen on FAF in the periphery in AMD and suggest that, like patterns observed by conventional means in the central 30, FAF patterns in the periphery can be predictive of disease progression.

Figure 6, although not an image from the above-referenced study, demonstrates what UWF FAF can reveal.

The clinical relevance of Optos UWF FA-identified retinal vascular nonprofusion in recalcitrant DME was underscored by a retrospective observational study published in the American Journal of Ophthalmology. These results suggested that patients with the largest areas of untreated retinal ischemia (as evaluated by calculating an ischemic index) and more severe DR were most likely to have DME that was unresponsive to established therapy, supporting the hypothesis that areas of nonperfusion may produce biochemical mediators (such as VEGF) of disease progression. This observation suggests that UWF FA could be used to determine which patients with recalcitrant DME might benefit from targeted retinal photocoagulation of untreated areas of nonperfusion and that an ischemic index may be useful in determining the necessary frequency of anti-VEGF therapy. As in other reports described here, the authors call for randomized, prospective studies to confirm their findings.

Figure 7 shows an example of how UWF FA can show peripheral vascular fronds accompanied with areas of ischemia.

Work by Paul Tornambe, MD, and colleagues in San Diego has raised similar fundamental questions about DME. Based on evidence from UWF images, they propose that DME is principally a peripheral retinal disease, which only secondarily involves the macula. Furthermore, their findings also suggest that targeting the periphery can reduce or stop VEGF production, not simply block its effects. This hypothesis that laser photocoagulation should be targeted at the periphery to decrease the VEGF load is likely to encourage a reevaluation of the relationship between VEGF inhibitors and grid (scatter) photocoagulation in the treatment of DME. Several of their cases suggest that targeted laser photocoagulation to the midperiphery and periphery decreases severe DME by reducing VEGF production in the ischemic retina, while also reducing the number of intravitreal anti-VEGF injections needed.

Michael Singer and colleagues have been using UWF FA to evaluate the extent of peripheral nonperfusion in patients with branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO). They observed that extensive peripheral nonperfusion may be present in eyes with venous occlusive disease (beyond the ETDRS 7-field territory), noting that the extent of nonperfusion appeared to be quite variable but did not significantly affect the durability of therapy. Eyes with more severe ischemia appeared to have more macular edema but also demonstrated a greater reduction with treatment. The authors suggest that their findings underscore the role UWF FA could play in guiding therapy with VEGF inhibitors and laser photocoagulation, as well as the importance of incorporating UWF imaging in future clinical trials.

Summary

This is an exciting time to be a vitreoretinal specialist. We are making major strides in the classification, early identification and effective management of most sight-

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threatening retinal diseases. With these advances, it has become increasingly evident that the retinal periphery may hold critical clues to both the disease process and treatment success and that the key to visualizing and evaluating peripheral pathology is UWF imaging. A significant amount of work is going on to validate and expand on these observations. One gauge of the level of global clinical interest and activity in this area is the fact that the last two Association for Research in Vision and Ophthalmology Annual Meetings (2012 and 2013) saw the presentation of a combined total of approximately 100 posters and talks based on research involving Optos UWF technology. As UWF imaging becomes a standardized component of research protocols evaluating new treatment approaches, it will inevitably be incorporated into normal clinical practice, from periodic exams to treatment outcomes monitoring. Our UWF view of the retina will enable more rapid progress in understanding retinal pathology and greater success preventing or managing it in each individual patient. Although it may be too soon to call UWF imaging technology indispensable for the retina practice, that day is most likely not so far in the future.

Szilárd Kiss, MD, is an Assistant Professor of Ophthalmology and Director of Research at Weill Cornell Medical College and an Assistant Attending Physician at the New York Presbyterian Hospital in New York. Dr. Kiss is a consultant to Optos, and his institution has received research funding from the company. He reports no financial interest in the technologies discussed. He may be reached at szk7001@med.cornell.edu.