Fluorescein Angiography in 2008

What is the role of this imaging modality in today's retinal practice?

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The current role for fluorescein angiography (FA) in a busy retinal specialist's practice is under vigorous debate as optical coherence tomography (OCT) technologies have improved. In this article, we outline the current indications for using FA and discuss how spectral-domain (SD) OCT is revolutionizing treatment, how FA imaging may evolve in the future, and the value of FA to today's practice.

POSITION OF FA IN RETINAL IMAGING

The role of FA is rapidly changing as OCT technologies are becoming more available to retina specialists. Even so, FA will continue to be crucial in the diagnosis and management of many retinal diseases, particularly in retinovascular disease and age-related macular degeneration (AMD).

As a dynamic imaging modality that visualizes the vascular components of the retina and active leakage of the blood-retinal barrier, FA remains an essential diagnostic tool. FA is the mainstay for diagnosis of retinovascular diseases, including central/branch retinal artery/vein occlusion, hypertensive and radiation retinopathy, idiopathic juxtafoveal telangiectasis, and Coats' disease, to name a few. In inflammatory diseases, leakage of fluorescein around the optic nerve head, in areas of vasculitis, and from cystoid macular edema seen on FA all can help with diagnosis and affect patient management. Documentation of choroidal neovascularization (CNV) in AMD, myopic degeneration, histoplasmosis, and other conditions that induce CNV remains a driving force behind the continued use of FA.

For macular degeneration, FA is an indispensable initial diagnostic tool because it can document the presence of CNV. The type, size, and composition (ie, classic, occult, or retinal angiomatous proliferation) of CNV can be determined. In the era of photodynamic therapy, FA was typically required for retreatment decisions.[1]

Now, however, antiangiogenic drugs have become the mainstay of AMD treatment. They block both the angiogenic and vascular permeability aspects of vascular endothelial growth factor (VEGF).[2-4] Once therapy is initiated with intravitreal agents, on follow-up visits the primary decision for the retina specialist becomes whether or not to re-treat. The most common deciding factor in the retreatment decision typically is whether there is active leakage; the presence of intraretinal fluid, subretinal fluid, and pigment epithelial detachment (PED) are all markers for disease activity.

Optical coherence tomography can accurately measure the macular volume and reliably track changes in retinal thickness over time, with changes in retinal thickness detected as low as 3 µm using the latest ultrahigh-resolution devices.[3-5] In the PrONTO study (Prospective OCT Imaging of Patients with Neovascular AMD Treated

with Intra-Ocular Ranibizumab), the retreatment decision was guided by OCT, not FA. Criteria for retreatment were a loss of five letters in conjunction with fluid in the macula as detected by OCT, an increase in OCT central retinal thickness of ≥100 µm, new-onset classic CNV, new macular hemorrhage, or persistent macular fluid detected by OCT at least 1 month after the previous injection of ranibizumab. Visual acuity outcomes of PrONTO were similar to the MARINA (Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD) and ANCHOR (Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in AMD) phase 3 trials but cut the frequency of dosing from 12 to about five injections per year.[4,5] Based on these and other results, OCT appears to be a highly effective tool for guiding retreatment decisions for patients with neovascular AMD and may allow greater individualization of dosing intervals. Many retinal specialists are shifting to OCT as the exclusive modality for follow-up treatment decisions.

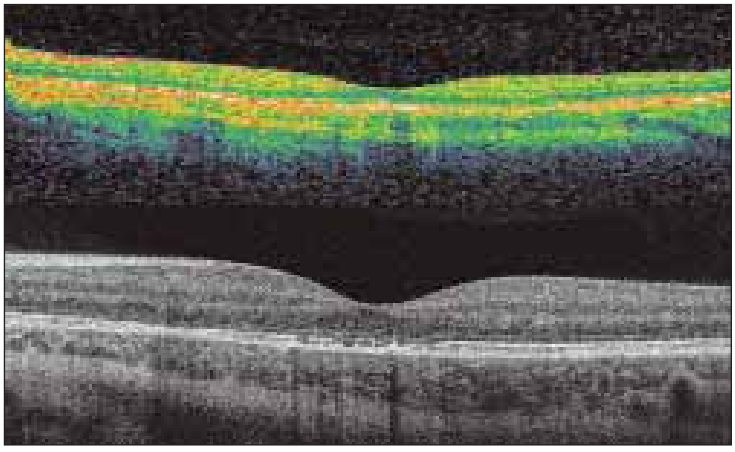

Figure 1. The difference in detail of the retinal layers is dramatic between TD OCT (top) and SD OCT (bottom). Both images are horizontal scans of the same eye taken on the same day.

Some have argued for repeating the FA prior to halting monthly intravitreal injections, even if the OCT is devoid of fluid. Subgroup analysis from the PIER (A Phase IIIb, Multicenter, Randomized, Double-Masked, Sham Injection-Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovascularization with or without Classic CNV Secondary to Age-Related Macular Degeneration) trial suggests that patients who underwent quarterly injections with no evidence of fluid on OCT were more likely to gain acuity if the FA also showed no evidence of leakage.[5]

The optimal dosing strategy for anti-VEGF medications is still under debate. Although FA remains important for initial documentation of CNV, OCT has increasingly supplanted FA in retreatment decisions.

SAFETY PROFILE: FA VS OCT

The increasing use of OCT instead of FA is also based in part on the safety and convenience of using OCT. While fluorescein is a relatively safe, US Food and Drug Administration-approved drug for angioscopy, FA is not a benign procedure. Risks from intravenous usage include mild vasovagal reactions (<10% of injections), severe vasovagal reactions, urticarial reactions (about 1% of injections), anaphylactic reactions/cardiovascular shock (less than 1 in 100,000 injections), and reactions from local dye extravasation at the injection site.[6] Also, fluorescein can be transmitted through breast milk in lactating women. Although there has been no evidence of teratogenic effects from fluorescein, many retina specialists attempt to avoid performing FA in pregnant women.[7,8]

Optical coherence tomography has several distinct advantages over FA as a diagnostic procedure: it is noninvasive, safer and more comfortable for patients, quicker to perform, less demanding on support staff, and consumes less supplies. The trend in OCT supplanting FA as a diagnostic procedure is likely to increase.

SPECTRAL-DOMAIN VS TIME-DOMAIN OCT

Recent improvements in OCT technology have also increased its attractiveness. Time-domain (TD) OCT, is the more commonly available, older technology that typically records data in six 6-mm image radial slices through the macula, with each image offset by 30º. Because intervening retinal areas are interpolated, important pathology may be missed with TD OCT. Additionally, TD OCT lacks precise registration of images, so fixation may affect reproducibility.

Spectral-domain OCT is a newer, albeit more costly, OCT technology that has become increasingly available. SD OCT differs from TD OCT technology in that design improvements have allowed greater imaging speed and better resolution.[9] Greater speed means less movement artifact, enhanced comfort for the patient, and an ability to generate superior detailed 3-D images. SD OCT typically acquires a 6x6 mm volume of tissue rather than just six slices. Precise registration allows comparison of the same retinal structures from different patient visits. The improved resolution also

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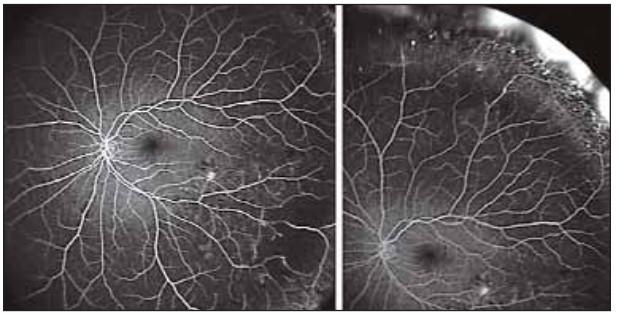

Figure 2. Example of view possible with Staurenghi wide angle lens for fluorescein angiography. Fluorescein angiographic images of a 38-year-old man with Behçet disease. Widefield scanning laser ophthalmoscope (SLO) angiography reveals areas of capillary nonperfusion and extensive retinal neovascularization well beyond the imaging fields of conventional fundus cameras and SLOs.

allows finer details of retinal layers to be examined, such as the photoreceptor inner segment/outer segment junction (Figure 1).

Spectral-domain OCT's ability to achieve near-histologic resolution and 3-D point-to-point correlation between images has led to suggestions that SD OCT may supersede FA in diagnosis and pathology differentiation. Given these improvements over TD OCT and despite the additional cost, SD OCT is rapidly moving from the academic to the private-practice setting and gradually replacing TD OCT. Improved image resolution, speed, and registration of SD OCT only encourage further adoption of this technology.

IMPROVEMENTS TO FA

Today, improvements to traditional FA techniques are focused on improving standalone FA image capture and combining the SD OCT with FA technologies. Many of these technologies, despite a substantial price tag, are now available for private-practice use.

Wide-angle, panoramic views of the retina during FA are now possible with several technologies. Widefield contact lens systems, such as the Staurenghi lens,[10] and scanning digital ophthalmoscopes, such as the Optos P200A/Optomap system (Optos, Fife, United Kingdom), can enable views of the peripheral retina during FA (Figure 2).[11] This technology may find increasing use for diabetic retinopathy, sickle cell disease, and other peripheral retinovascular pathology.

Other FA innovations focus on providing the clinician with simultaneous OCT and FA image capture. Systems such as the Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) can capture OCT and FA images concurrently and use FA images as references to the SD OCT volume scans. Using these systems, clinicians can obtain point-to-point correlation between OCT and FA with the practical convenience of achieving multiple scans performed at one station during a single sitting.

VALUE OF FA IN RETINA PRACTICE

There is no doubt that FA will remain an indispensable imaging tool for retina specialists in the diagnosis and management of a multitude of retinal disorders. Further advances in FA imaging technology will expand its usefulness, such as widefield panoramic viewing and combination systems that can overlay images from multiple modalities. Clearly, the use of OCT has increased exponentially due to the high-resolution, near-histologic images it provides, combined with its noninvasive nature, safety, and ease of use. OCT has displaced FA in a number of areas as the imaging modality of choice. However, the two technologies provide complementary information, and retina specialists will continue to rely on FA for the foreseeable future. ■

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