Early Detection and Better Results for AMD

The Foresee PHP is an important tool for determining the conversion to neovascular AMD.

BY DIANA REEVES, MD

How important is early detection of exudative age-related macular degeneration (AMD)?

This question can be answered by examining data from 53 primary studies conducted between 1980 and 2005 on 4,362 untreated neovascular AMD patients (n=36% classic, 31% occult, 81% subfoveal). A compilation of the study results showed an average of one line of visual loss at 3 months, three lines at 12 months, and four lines at 24 months for these untreated patients. More importantly, severe visual loss (ie, >6 lines) occurred in 21% of the patients at 6 months and 42% of patients at 3 years.[1]

This proves, without any doubt, that the early detection of exudative AMD is vital in order to preserve vision by initiating prompt treatment (Figures 1 and 2).

EARLY DETECTION

Early detection, however, has been a challenge for the general ophthalmic community. Patients with macular degeneration may suffer from a variety of other ocular conditions (eg, cataracts, dry eye, atrophic macular changes), which make a slight change in vision related to the development of neovascular disease, difficult to diag-

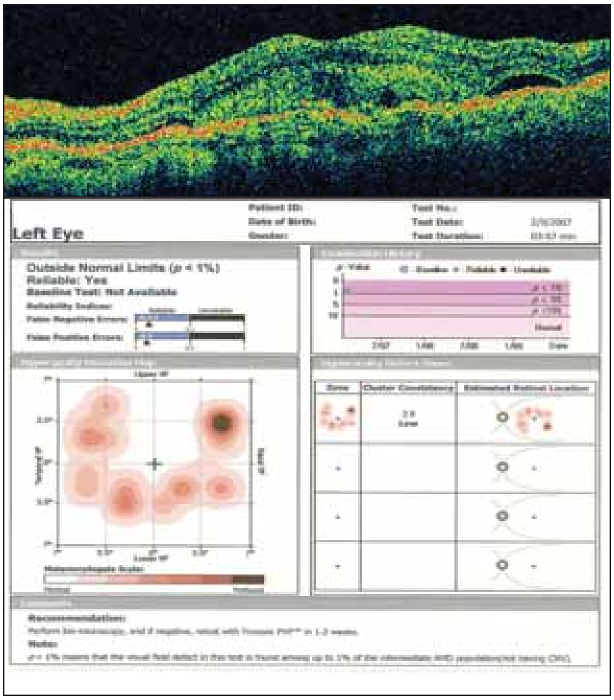

Figure 1. Preferential hyperacuity perimeter (PHP) and optical coherence tomography (OCT) correlate in identifying exudative AMD. PHP localizes the area of leakage within the macula.

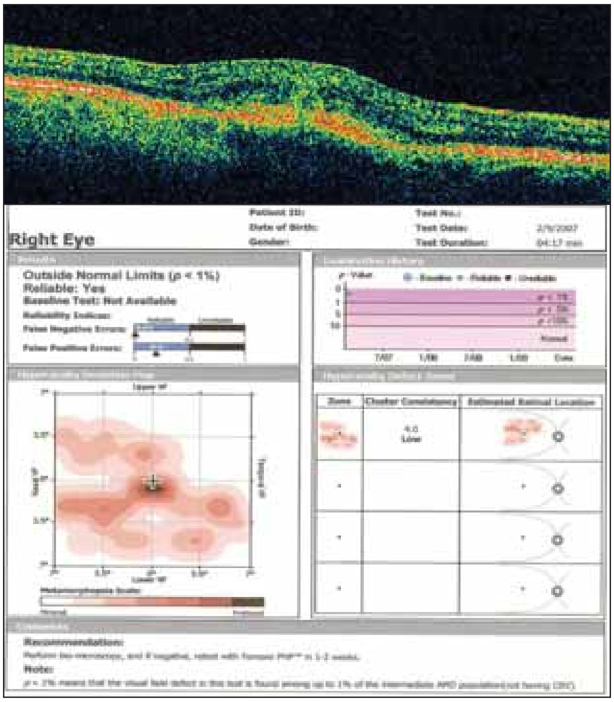

Figure 2. The PHP reading strongly suggests that the OCT shows a neovascular process.

nose. Additionally, patient self-monitoring using the Amsler grid is often inadequate because the brain typically compensates for retinal defects. In my experience, the transition to early exudative disease is not recognized soon enough in approximately 15% of patients.

In spite of these factors, recent advancements in drug treatments and diagnostic technology make the present an exciting time for the AMD community. One such technology showing exceptional promise is the Foresee PHP (preferential hyperacuity perimeter) (Notal Vision, Tel Aviv, Israel), a device designed for early diagnosis of choroidal neovascular membrane.[2] The Foresee PHP is the follow-up to the Preview PHP (Notal Vision), the only ophthalmic device to receive US Food and Drug Administration clearance for monitoring the progression of AMD. It allows eye care professionals to track a patient's visual field for changes characteristic of exudative disease. The device administers an easy-to-perform test, which identifies characteristic elevations in the retinal pigment epithelium that are consistent with conversion to exudative AMD.

The Foresee PHP's diagnostic capability is based on the phenomenon of hyperacuity, defined as the ability to perceive a minute difference in the relative spatial localization of two or more visual stimuli. The test maps defects within a patient's visual field by analyzing responses to dot deviation signals that flash on a computer screen. Practically, a signal (closely spaced dots) is

OPTICAL COHERENCE TOMOGRAPHY PRODUCT GUIDE

Information provided by industry representatives.

Bioptigen, Inc.

Spectral Domain Optical Coherence Tomography (SDOCT) (Bioptigen, Research Triangle Park, NC) is a second-generation imaging technology that will change the face of ophthalmic disease management. Optical coherence tomography (OCT) was originally invented at the Massachusetts Institute of Technology in the early 1990s and is attractive for its ability to generate depth-resolved images of ocular structures in vivo and without physical contact. OCT has become a standard of care in ophthalmic diagnostics, but has been generally relegated to diagnostic applications of postsymptomatic patients. We believe that due to its greater imaging speed, finer resolution, and volumetric imaging capability, SDOCT systems will soon displace older OCT systems.

SDOCT has a 100-fold signal-to-noise advantage over first-generation technology, immediately translating to faster imaging (Figure 1). Where first-generation systems acquired images at 400 depth-resolved lines per second, spectral domain systems acquire images at 20,000 lines per second and more. There are immediate advantages to this speed increase. High-resolution cross-sectional images (ie, B-scans) can be acquired at video rates, and three-dimensional images—not even feasible with last-generation technology—can be acquired in the blink of an eye. These acquisition speeds freeze artifacts of motion for a doubling of effective axial resolution, significantly increasing the clarity of retinal physiology and eliminating the need to artificially normalize distortions of B-scans that are caused motion. At these imaging speeds, the emphasis rapidly shifts to resolution and image quality.

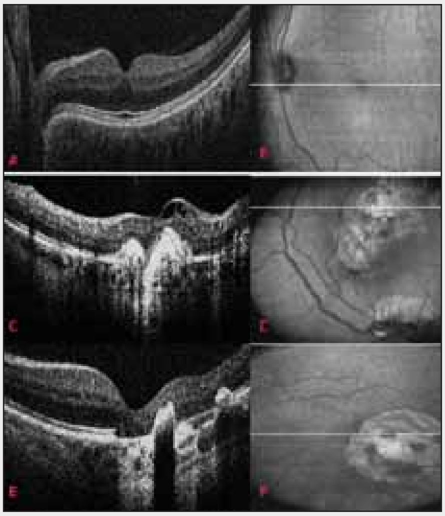

Figure 1. Images of human retina, illustrating the utility of Bioptigen's 840 nm imaging system in resolving fine layers of normal and diseased human retina. The images on the left (A, C, E) are selected B-scans from three patients. Images on the right (B, D, F) show the en face image from each of those patients. Images A and B are from a healthy patient, while images C, D, E, and F are from patients with AMD.

Bioptigen SDOCT (Figure 2) provides the highest-resolution imaging for diagnostic and research applications. Resolving power is critical for assessing early symptoms of eye disease, whether the formation of drusen, the onset of choroidal neovascularization, or fractional changes in retinal edema or retinal nerve fiber layer thicknesses. Bioptigen systems provide ≥6 µm resolution, independent of depth. One setting provides exceptional image clarity for analyzing the retina from retinal nerve fiber layer through choriocapillaris; flexibility is provided for imaging the deepest optical nerve head cups. Furthermore, the Bioptigen system is compatible with very broadband sources, providing resolution >3 µm, with no other hardware modification; ultra-high resolution sources are available upon displayed on the device's screen for 160 ms. Patients use a stylus pen to touch the screen to identify the most prominent distortion in the line. A typical 3- to 5-minute test measures 500 retinal data points covering the central 14° of the macular visual field. The response patterns are recorded, analyzed, and compared to the normative database, producing a report that reveals the relative location of defects in the macular area.

The PHP system builds a topographic map of the patient's vision to highlight all areas of concern in the macula. In that respect, it differs from optical coherence tomography (OCT), which gives a cross-section snapshot through the point of fixation. When multicentric disease is present, OCT will not pick up all of the areas that show exudation. On the other hand, the pattern of dye leakage on angiography can often be confusing. PHP will help delineate if there is more exudation in the overall lesion. A patient who has been receiving treatment can suspend treatments if all the areas of exudation are dry. PHP used in combination with OCT may also help to minimize the use of angiography during follow-up.

All AMD patients should have a baseline PHP. Then, depending on the absence or presence of high-risk features for neovascular disease, repeat testing may be performed anywhere from 2 to 4 times a year. There are few false-positive results with PHP, but, like every other test, the information provided has to make sense in the

Figure 2. Bioptigen SDOCT clinical scanner and software interface, showing retinal B-scan, en face image, and fixation target.

request as an upgrade. Bioptigen systems are ideally suited for glaucoma and macular analysis and for tracking disease change in coordination with drug, laser, or surgical therapy.

In addition to a chin-rest–clinical scanner for imaging of mobile adult patients, Bioptigen offers hand-held scanning probes and SDOCT microscopes for imaging disabled or immobile, neonatal and pediatric patients. The hand-held probe and microscopy systems provide additional utility for imaging nonclinical subjects (eg, rodents, larger animals) and for ex vivo ocular tissue analysis. The Bioptigen imaging platform is equally suitable for high-resolution anterior imaging of the cornea, sclera, conjunctiva, and tear films with the addition of accessory optics.

Both the clinical scanner and the hand-held probes provide the ability to image from the cornea apex to the ocular angle, for cornea images, and images of Schlemm's canal.

Bioptigen provides a software system with flexible workflow and advanced visualization capabilities. Preprogrammed scan modes support routine glaucoma and retinal diagnostics, whereas user-defined scan modes with up to 10,000 lines per B-scan and volumes to 512 X 512 X 1024 pixels, allow for more specialized investigations. During aiming mode, an integrated iris/fundus camera allows the photographer to rapidly align and zoom in on the patient's retina. A two-axis B-scan image comes into view as the fundus comes in focus. The photographer guides the patient's gaze using a continuously variable fixation target to precisely locate the pathology of interest. During acquisition mode, fully processed B-scans and volume intensity projections (ie, face images derived from volumetric SDOCT images) are displayed in real-time, with 1,000 line frames displayed at 17 frames per second. This display ensures that image location and quality are optimal, reducing the time required for review and remeasurements.

The system is integrated with multiple two- and three-dimensional visualization and measurement modes. In addition, Bioptigen offers the first OCT-based functional imaging capabilities. Doppler processing provides information on patterns of blood flow in the retinal vascular system. Bioptigen's programmable fixation target provides dynamic capability for retinal excitation imaging. Processed SDOCT images, bitmaps of the video fundus, and raw data directly from the spectrometer are saved in an easily managed, user-accessible database.

In the short term, SDOCT will displace first-generation OCT for its faster imaging speed and improved image quality. Over time, look for SDOCT to become a standard in computer-aided diagnostics and image-guided therapy, with both structural and functional imaging.

For more information, visit www.bioptigen.com. ■

clinical context. PHP offers a technique to diagnose neovascular AMD with about 85% sensitivity and 88% specificity.[2]

For patients who convert from nonneovascular to neovascular AMD, two key factors determine the outcome, (1) disease stage at diagnosis and (2) prompt treatment. Treatment results are contingent on timely diagnosis. Currently, from my experience, retinal specialists receive approximately 30% of AMD referrals too early; these patients have nonneovascular disease, for which there is no current treatment. Approximately 15% of patients are being referred too late; they have severe, irreversible vision loss for which treatment has minimal impact. Ideally, diagnosis and treatment should occur right after conversion to neovascular AMD, before

Figure 3. The Foresee PHP.

NEW TECHNOLOGY COMBINES OCT WITH ANGIOGRAPHY

Information provided by industry representatives.

Heidelberg Engineering GmbH

In November 2006, Heidelberg Engineering introduced Spectralis HRA+OCT—a commercial spectral domain optical coherence tomograph (SD-OCT) that can image simultaneously with laser angiography. The new system combines Heidelberg Engineering's TrueTrack image alignment technology found in the Heidelberg Retina Tomograph II (HRT-II) and Heidelberg Retina Angiograph (HRA) (both Heidelberg Engineering GmbH, Heidelberg, Germany) products, with second-generation OCT technology, overcoming many of the limitations found in older time-domain OCT systems.

Spectralis' ability to capture OCT and HRA images simultaneously provides clinicians precise accounts of the exact location of an area of interest, and it correlates the outer visible retina structure with the internal structure (Figure 1). The new technology has already shown previously unrecognized structures, combining high-resolution cross-sectional images of the retina with any of five imaging modalities: ICG angiography (Figure 2), autofluorescence, red free, infrared, or fluorescein angiography. The new device scans the retina 100 times faster than time domain OCT.

The Spectralis can gather 40,000 A-scans per second. The high speed and noise-reduction technology enable ultra-high resolution images, revealing all of the individual layers of the retina. In addition to high-performing OCT scans, the Spectralis includes all of the fundus imaging features of the company's scanning laser ophthalmoscope (ie, motion picture angiography, real-time wide-field imaging, noise reduction, fundus autofluorescence) providing new diagnostic dimensions over traditional photography.

Of recent interest is the HRA's capability to cause certain retinal components to fluoresce in a process known as autofluorescence (Figure 3). Geographic atrophy of age-related macular degeneration (AMD) is being followed using autofluorescence as a potential early indicator of disease progression in the recently announced Age-Related Eye Disease Study (AREDS 2) clinical trial. Although traditional fundus cameras have been modified to show autofluorescence and indocyanine green (ICG) angiography, it is the use of laser light in the HRA that has allowed clinicians to capture crisp images of both the fundus and the choroidal blood vessel structure within the retina; both key diagnostic indicators for such common eye diseases as AMD and diabetic maculopathy.

SPECTRALIS KEY FEATURES

Eye Tracking. Spectralis locks onto the patient's eye and follows it, eliminating much of the artifact due to eye movement. Eye tracking is necessary for obtaining high quality

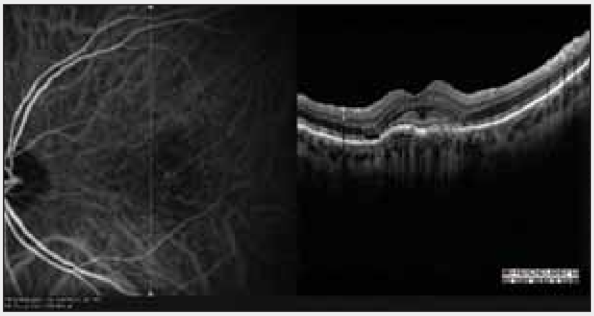

Figure 1. Indocyanine green angiography (ICGA) image of occult choroidal neovascularization (CNV).

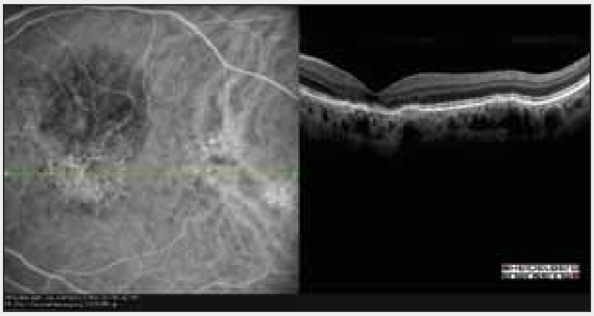

Figure 2. ICGA image of CNV with choroidal hemangioma.

vision loss has occurred.

PHP is an important tool in the comprehensive eye care doctor's office for determining the conversion to neovascular disease and helping to make the decision to ask for a retinal consult thus minimizing the doctor's liability. PHP information complements the existing retinal tests used by the retinal specialists in order to make a complex diagnostic and appropriate treatment decision. PHP is complementary to traditional OCT and fluorescein angiography to help guide decisions about retreatment, especially in patients with extensive macular disease. ■

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2. Preferential Hyperacuity Perimetry Research Group. Preferential Hyperacuity Perimeter (PreView PHP) for detecting choroidal neovascularization study. *Ophthalmology.* 2005;112:1758-1765.

HEIDELBERG SPECTRALIS

***Spectralis* OCT (two modes)**
- OCT
- Infrared

***Spectralis* HRA (five modes)**
- Infrared
- Autofluorescence
- Flourescein Angiography
- ICG Angiography
- Red-Free Photography

***Spectralis* HRA+OCT (six modes)**
- OCT
- Infrared
- Autofluorescence
- Flourescein Angiography
- ICG Angiography
- Red-Free Photography

images, especially in elderly patients with pathology who have trouble fixating (Figure 3).

Simultaneous Imaging. All Spectralis cross-sectional images are obtained simultaneous to a fundus image. This allows the clinician to know the exact location of the OCT scan relative to the appearance of the lesion on the surface of the retina.

Six Available Modes. Multiple perspectives of the anatomy from multiple wavelengths: fluorescein angiography, ICG angiography, autoflorescence, red free, infrared and OCT.

TruTrack Image Alignment. A proprietary method of automatically aligning images using 600 matching points of anatomical structure and image characteristics. TruTrack technology is used for aligning images in the same exam and for finding the same location in subsequent exams, creating accurate and repeatable reference points. This enables Spectralis and other Heidelberg instruments to accurately track subtle change over time.

40k-Hz Scanning. High speed helps overcome eye-movement artifact and provides crisp images. It also speeds the imaging process, increasing patient comfort.

Heidelberg Noise Reduction Technology. Stems from the eye-tracking software's ability to register the retina, which allows the Spectralis to take multiple B-scans in the same location. The scans are instantly aligned and the speckle is eliminated. The result is high-quality images (Figure 4) compared to high-resolution images without noise reduction. For more information, visit visit www.HeidelbergEngineering.com ■

(Six applicable US reimbursement CPT codes: 92135, 92235, 92240, 92250, 92285, 92287.)

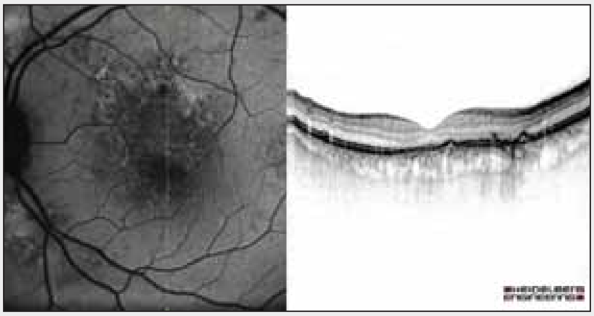

Figure 3. Flourescein angiography image with CNV and macular choroidal hemangioma.

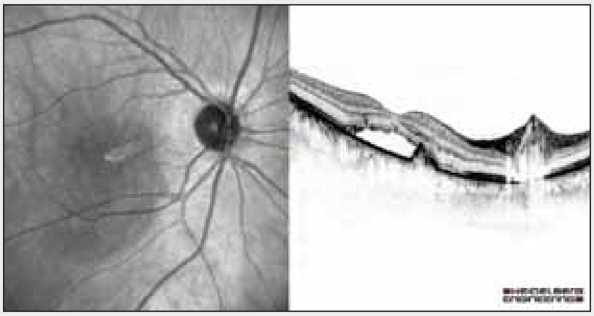

Figure 4. Infrared image with central serous chorioretinopathy.