

INNOVATIONS IN GLAUCOMA DIAGNOSTICS



A survey of new and next-generation technologies and devices.

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Worldwide, the number of people with glaucoma is expected to increase from 76 million to 111 million between 2020 and 2040.¹

If previous estimates are accurate, then more than 50% of patients with glaucoma will go undiagnosed and 13.5% will go blind in one eye.^{2,3} Although these numbers are staggering, new surgical and medical innovations in the treatment of glaucoma are enabling eye care practitioners to fight back against glaucomatous vision loss. Equally important are the new diagnostic technologies helping us to accurately detect and monitor this disease

so that we can appropriately treat our patients. This article provides a review of these diagnostic discoveries.

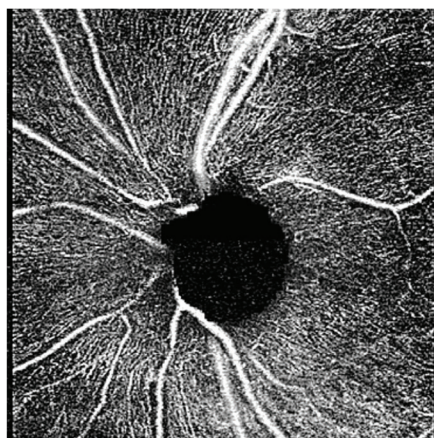
OCT

OCT has revolutionized the management of glaucoma by allowing us to quantitatively measure the peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell-inner plexiform layer (GC-IPL) thicknesses in vivo. Both measurements improve the detection of glaucoma, especially in early to moderate cases. After disease diagnosis, both measurements can be used to monitor for progressive glaucomatous changes. Eye care practitioners often

gravitate toward these quantitative metrics of glaucomatous disease because of their impressive clinical utility, but OCT is capable of much more than simple thickness analysis.

Although the lamina cribrosa cannot be visualized with funduscopy, evaluation of various laminar features (ie, laminar thickness and curvature) is possible with enhanced depth imaging-OCT (EDI-OCT). In studies comparing normal patients to patients with glaucoma, those with glaucoma had statistically thinner laminar thickness measurements, as noted with OCT.⁴ Laminar thickness also correlated with the amount of visual field loss; patients

Radial Peripapillary Capillaries Slab



RNFL Thickness

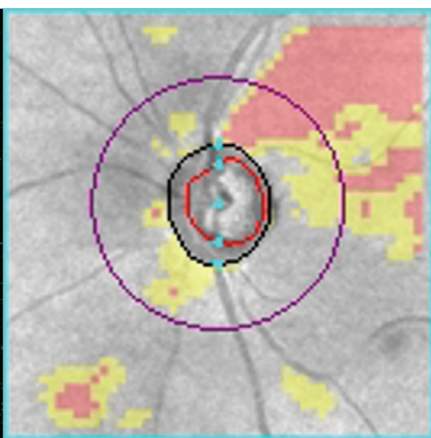


Figure 1. OCT-A reveals radial peripapillary capillary relative nonperfusion superior-temporally, which correlates with RNFL thinning superior temporally.

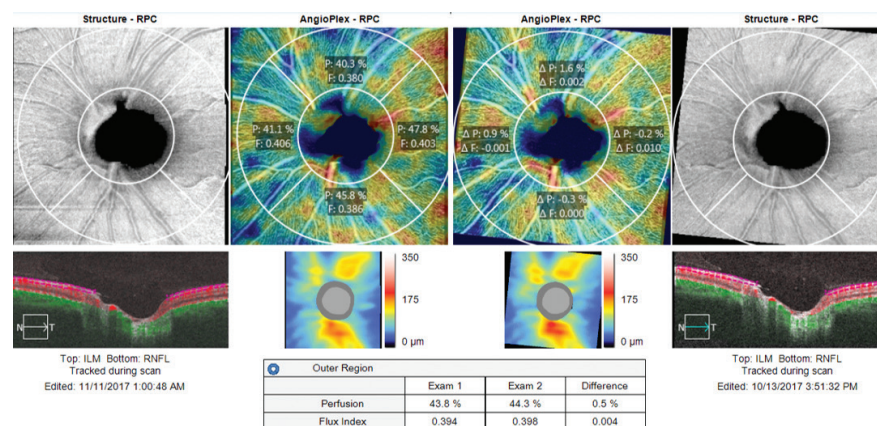


Figure 2. OCT-A quantification and progression analysis. Note: Not available in the United States, but approved for clinical use in Europe.

with more advanced glaucoma had thinner laminae.⁵ As glaucomatous axonal degeneration develops, axonal apoptosis and posterior laminar deformation lead to the clinical sign of cupping. The surrogate for axonal apoptosis is measured with our standard RNFL and GC-IPL measurements, but there is still no commercially available metric for laminar curvature.

Researchers have used laminar curvature and its progressive posterior deformation in patients with glaucoma as a metric for the detection of glaucoma and as a predictor of progression rate. In patients with glaucoma, the lamina cribrosa was located more posteriorly as compared to controls.⁶ Eyes that had greater increases in posterior deformation of the lamina cribrosa also had greater rates of visual field progression.⁷ Likewise, eyes with greater laminar depth had a faster rate of RNFL thinning.⁸ We are only able to detect structural glaucomatous change once atrophy sets in, but measurements of the lamina cribrosa may one day provide clinical data before cell loss begins.

OCT Angiography

Until recently, it was difficult to study the microvascular structure of the retina and optic nerve head (ONH) due to the resolution limitations of fluorescein angiography. Since the invention of OCT angiography (OCT-A), researchers have been able to investigate in vivo vascular changes of the ONH and macula in patients with glaucoma in greater detail than ever before. The loss of peripapillary vessels, particularly the radial peripapillary capillaries that nourish the RNFL, colocalize with OCT RNFL thinning and visual field defects (Figure 1).

Although RNFL thickness measurements tend to detect glaucoma better than OCT-A measurements, visual field defects correlate better with OCT-A measurements. In one study, the improved correlation of OCT-A and perimetry was especially apparent in advanced glaucoma, where RNFL thickness measurements reach a floor

AT A GLANCE

- OCT-A provides an objective functional component to the glaucoma diagnostic armamentarium.
- Higher corneal hysteresis is linked to a lower probability of developing glaucoma and a higher maintained visual field index over time.
- One of the newest breakthroughs in perimetry is testing performed through virtual reality headsets, which correlate to Humphrey fields, are available at a lower price point, and allow out-of-office examination.
- Home-based IOP measurement is the largest area of opportunity for innovation.

Photo courtesy of iCare USA.



Figure 3. The iCare Home tonometer allows patients to measure IOP at home.

Photo courtesy of Olleyes.



Figure 6. The VisuALL VR visual field perimeter was designed for standardized and mobile assessment of the visual field.

effect earlier than OCT-A.⁹ Vessel densities of the macula have poorer glaucoma detection capabilities than peripapillary OCT-A measurements, but can be used as complementary data analogous to GC-IPL thickness measurements. It is unclear whether vascular changes within the posterior pole are occurring before, during, or after structural glaucoma changes, but it is clear that OCT-A measurements provide an objective functional component to our glaucoma diagnostic armamentarium (Figure 2).

Adaptive Optics

Spectral domain OCT scans have impeccable clarity in the axial direction, but are limited in the lateral direction secondary to aberrations. Adaptive optics can resolve those aberrations, allowing more detailed views of retinal tissue and earlier detection of damage. However, current challenges of this technology include its cost, limited depth of focus and field of view, speed of testing, and the need for extensive training and specific interpretation tools.^{7,8}

Photo courtesy of Implants Ophthalmic Products.



Figure 4. The Eyemate system works using a pressure sensor that is implanted during cataract surgery.



Figure 7. Re:Vive 2.0 features six diagnostic exams with five existing CPT codes in one wearable visual field testing unit.

TONOMETRY

The largest area of innovation in tonometry is home-based IOP measurements. In the past, eye care providers were only able to get a snapshot of a patient's IOP while they were in the office, which does not account for the natural diurnal curve that results in higher IOP while sleeping and in the early morning hours. These diurnal fluctuations tend to be higher in patients with glaucoma and ocular hypertension, which raises their risk of progression.⁹⁻¹² New devices, such as the iCare Home tonometer (iCare USA; Figure 3); the Sensimed Triggerfish (Sensimed), which is not commercially available; and the Eyemate system (Implandata Ophthalmic Products; Figure 4), which is only approved in Europe, allow out-of-office measurements that reflect the peaks and troughs of a patient's pressures and can be used for customized treatment plans.

CORNEAL HYSTERESIS

Measured with the Ocular Response Analyzer (ORA) G3



Photo courtesy of Reichert Technologies.

Figure 5. The ORA G3 measures CH and corneal compensated IOP.

(Reichert Technologies; Figure 5), *corneal hysteresis* (CH) is the difference between the pressure at which the cornea bends inward during airjet applanation and the pressure at which the cornea bends out again. In other words, it is the measure of the viscoelasticity of the cornea that corresponds to its ability to dampen forces imposed upon it. Studies have demonstrated that higher CH is linked to a lower probability of developing glaucoma and a higher maintained visual field index over time, with current thought suggesting that CH mimics the flexibility within the lamina cribrosa and indicates the eye's capacity for shock absorption.^{13,14}

PERIMETRY

Contemporary diagnostic advancements have been made in two aspects of perimetry: testing pattern and remote testing.

24-2c

Traditionally, glaucoma visual fields have been performed using 24-2 and 30-2 patterns, which screen few points within the macular area. Donald C. Hood, PhD, found in 2013 that glaucomatous damage is often present within the macular area of glaucoma suspects and in every stage of the disease.¹⁵ In patients with mild glaucoma, it has been found that 15% of normal 24-2 fields have damage on a 10-2 test.¹⁵ The 24-2c test was developed based on these new data. The test includes 10 additional points within the macular area that follow the asymmetric

pattern of the bundle, testing the most vulnerable points.¹⁵

Virtual Reality Perimetry

One of the newest breakthroughs in perimetry is testing performed through virtual reality (VR) headsets. These tests correlate to Humphrey fields, are available at a lower price point, and can be more easily used by patients who are wheelchair-bound, bedridden, or have neck or back problems. Importantly, they also allow out-of-office examination, which provides an opportunity to perform serial testing at home and offer telehealth, leading to more accurate disease management.¹⁶⁻¹⁸

VisuALL (Olleyes; Figure 6) is a VR visual field perimeter designed for standardized and mobile assessment of the visual field. It automatically analyzes the retinal sensitivity in patients with glaucoma and other visual disorders and can examine multiple patients at a time for increased productivity.

Re:Vive 2.0 (Heru; Figure 7) is a wearable visual field testing unit that can be used in most lighting conditions to collect vital clinical data any time during a patient's visit. Re:Vive 2.0 features six diagnostic exams and five CPT codes.

ARTIFICIAL INTELLIGENCE

Glaucoma-related artificial intelligence (AI) is being developed to analyze and categorize data from testing, including fundus photos, perimetry, and OCT. These programs can be run supervised or unsupervised and are able to identify progression risk, disease stage, and recommend referrals. Although this technology is in its early stages and needs clearer definitions of the disease and normative data in order to be fully effective, AI will likely have a clinical role in screening large groups of patients to identify risks and trends and to recommend further testing in the future.¹⁹

“SINCE THE INVENTION OF OCT ANGIOGRAPHY (OCT-A), RESEARCHERS HAVE BEEN ABLE TO INVESTIGATE IN VIVO VASCULAR CHANGES OF THE ONH AND MACULA IN PATIENTS WITH GLAUCOMA IN GREATER DETAIL THAN EVER BEFORE.”

UPPING THE GLAUCOMA DETECTION GAME

Early detection of glaucomatous changes is imperative to the successful long-term management of this disease. With the introduction and implementation of innovations such as those described above, clinicians have an extensive and growing arsenal of testing with which to combat irreversible damage from this sight-threatening condition. ■

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