

EDITORIAL

Frequency Doubling Technology Perimetry for the Detection of Glaucomatous Visual Field Loss

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GLAUCOMA IS THE LEADING CAUSE OF IRREVERSIBLE blindness in the world.¹ It is estimated that 66.8 million people in the world have glaucoma, and of these, 6.7 million are bilaterally blind.¹ In the United States, approximately 2 million people have glaucoma and half are unaware that they are affected.²

Because glaucoma is a treatable disease, it is critical to identify affected individuals before they develop symptomatic vision loss. Unfortunately, glaucoma screening has been problematic. For decades ophthalmologists have searched for a screening tool that combines practicality with high sensitivity and specificity. The need for sensitivity is obvious; a screening test that fails to identify a significant proportion of affected individuals has little value. The need for specificity is less obvious but equally important, especially when testing a population in which the disease being screened for is not common. A glaucoma

See also pp. 314–322, 323–327, and 328–333.

screening test that is 100% sensitive and 90% specific would identify all patients with glaucoma but would also identify 10% of normal individuals as being affected. Those falsely identified would need to undergo further testing, and the cost of screening must include the cost of evaluating all individuals falsely identified as being affected. Any screening test will perform better if applied to a population in which the disease is more common. The prevalence of glaucoma among citizens of Baltimore, Maryland, aged 40 years and older is 1.7% for whites and 5.6% for blacks.³ In this population, our 90% specific test would identify as affected 100 normal individuals for every 17 white and every 56 black glaucoma-affected individuals. In other words, 5.9 normals would be falsely identified for every affected white patient versus 1.9 for every affected black patient. Therefore, the value of a screening test depends not only on the sensitivity and specificity of the

technique but also on the population to which the test is applied.

The sensitivity and specificity of tonometry, historically the most popular screening tool, are so poor that tonometry is virtually worthless by itself for screening.^{4,5} If an intraocular pressure of greater than 21 mm Hg were chosen as a screening cutoff, tonometry has a sensitivity of only 47.1% and a specificity of 92.4%.⁵ In other words, 52.9% of glaucoma patients would pass undetected through the screening exam. If the cutoff intraocular pressure level were decreased to greater than 17 mm Hg, the sensitivity would increase to 80.1% but the specificity would drop to 51.8%; almost half the normal population would fail the screen.⁵ There is no intraocular pressure that gives an acceptable balance of sensitivity and specificity. Optic nerve head examination requires an experienced examiner, has poor reproducibility and also has poor sensitivity and specificity.⁵ The gold standard for defining a patient as having glaucoma is usually visual field loss, typically tested on an automated static threshold perimeter such as a Humphrey Field Analyzer (HFA). Unfortunately, perimetric screening with the HFA has not been practical because the perimeter is expensive and not easily portable, test times are usually long, and there is a learning curve that may make the first test of limited value.⁵

Perimetry using frequency doubling technology (FDT) may provide a practical means of screening for glaucoma. In FDT perimetry, a cluster of 17 points is tested over the central 20 degrees of the visual field. Each test stimulus is a series of white and black bands that flicker at 25 Hz. The normal eye will perceive the illusion of twice the number of bands more closely spaced. It is not known whether eyes with visual damage still reliably see the doubled illusion. The test can be administered in a Full Threshold mode or a faster Suprathreshold Screening mode. In the Suprathreshold Screening mode FDT perimetry can test a normal eye in less than 90 seconds; the Full Threshold test requires about 5 minutes. The FDT perimeter is packaged in a portable and relatively inexpensive unit and the test is easily administered with a minimum of technical training. Additionally, the stimulus is resistant to blur up to about 6 diopters. Therefore, the patient can wear no glasses or

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regular distance vision lenses and does not need additional correction for near. Patients prefer FDT perimetry to traditional automated static threshold perimetry.⁶

Three papers in this issue of *THE JOURNAL* evaluate the ability of FDT to detect glaucomatous damage, using the HFA as a reference. Cello and associates describe a large sensitivity and specificity study.⁶ They tested 230 patients with varying degrees of glaucomatous damage and 254 normal subjects. The FDT perimeter was used in its Full Threshold mode and the findings were compared with the results obtained with a 30-2 Full Threshold test performed on the HFA. They found FDT perimetry to have 100% sensitivity and specificity for detecting advanced glaucoma, 96% sensitivity and specificity for detecting moderate glaucoma, and 85% sensitivity and 90% specificity for detecting early glaucoma. For each eye, the FDT test took 4.0 to 5.5 minutes to complete, compared with 12 to 20 minutes for the HFA.

Patel and associates used the FDT perimeter in the Screening mode and compared it with the HFA using the Swedish Interactive Threshold Algorithm (SITA) program.⁷ They developed an algorithm for grading the FDT results that emphasized points close to fixation and included information on the depth of field defects. They were able to demonstrate a sensitivity of 80% or greater and a specificity of 93% or greater for identifying patients with glaucoma. Sensitivity for detecting moderate to severe glaucoma increased to 95% with the same 93% specificity. The screening version of the FDT always took less than 90 seconds per eye if the patient did not have glaucoma. Once the test duration reached 90 seconds, it could be discontinued because the subject would have failed the screen.

Burnstein and associates studied 29 consecutive patients with glaucoma by means of FDT perimetry in both the Screening and Full Threshold modes.⁸ The results were compared with the 24-2 Full Threshold test on the HFA. They determined the sensitivity and specificity for FDT perimetry with a variety of definitions of abnormal. These results were compared with several methods of defining abnormality with the HFA. The highest sensitivity (100%) and specificity (90%) were found with the FDT perimeter in the Full Threshold mode, using the HFA Glaucoma Hemifield Test (GHT) as the reference standard. When other HFA parameters, mean defect and pattern standard deviation, were used as the reference standards the sensitivity and specificity were lower. The Screening mode was much faster, but at the expense of reduced sensitivity and specificity. Cello and associates have been working on increasing the speed of the Full Threshold FDT test using the same statistical maneuvers as are employed by the SITA program on the HFA.⁶ They have reduced the test time for the Full Threshold test to 2.0 to 2.5 minutes per eye.

These three studies show that FDT perimetry is an excellent tool for detecting patients with glaucoma. The

test is especially effective at detecting moderate or severe glaucoma, the groups most critical to identify. Frequency doubling technology perimetry may finally be a tool that can cost-effectively screen populations at risk.

Although the thrust of the three papers in this issue of *THE JOURNAL* is FDT perimetry for screening, the technique is also important because it may provide a better method to detect and follow glaucomatous damage than conventional achromatic (white-on-white) perimetry. Physicians have been measuring the visual field for over 200 years. Over the past several decades the major advances in perimetry have been in improving standardization of the testing experience. The Goldmann manual kinetic perimeter standardized testing distance, test object sizes, and the illumination of the test objects and the background. Armaly and Drance described standardized perimetric strategies for testing for glaucoma. More recently, automated static threshold perimeters have completely standardized the testing experience and virtually eliminated the variable of the perimetrist. Despite all of these advances, the state of visual field testing leaves a great deal of room for improvement. Most tests are slow, the machines are expensive and bulky, and a great deal of optic nerve damage must have occurred before any visual field loss was measurable.⁹

Recent perimetric development has turned from standardization and reproducibility to speed and sensitivity. The recognition that long test experiences are less reliable led to the development of SITA, which yields as much information as the Full Threshold test in about half the time.¹⁰ The search for improved sensitivity has moved perimetry away from the traditional system of testing with a white test object against a dim white background to the use of other stimuli that may be more sensitive to glaucomatous damage. Examples include short wavelength automated perimetry (SWAP),¹¹ random dot motion perimetry,¹² and FDT perimetry. Frequency doubling technology not only shortens test times but also theoretically selectively tests a limited portion of the visual system. The cells responsible for perceiving frequency doubling phenomenon are believed to be the My cells, a small subgroup of the magnocellular (M) cells.¹³ The M cells represent only about one tenth of ganglion cells and may be more sensitive to glaucomatous damage than the more numerous parvocellular (P) cells.¹⁴ The My cells represent only 25% of M cells and therefore only a tiny fraction of all ganglion cells. Whether the My cells are psychophysically isolated in eyes with visual damage is unproven; however, if the cells are isolated, selective studying My cells may be a sensitive means of detecting glaucoma, because these cells may be preferentially damaged, there is less redundancy in the My system, or both. Someday, variations of FDT perimetry may be used not only for screening but also for early diagnosis and follow-up of glaucoma suspects and confirmed glaucoma patients. The FDT perimetry has been tested in a 54 stimulus 24-2 pattern and provided slightly higher sensitivity and better characterization of

field loss than the standard 17 stimulus test.¹⁵ This came at the expense of doubled test time. We will need to determine how much long-term fluctuation is present in the test to decide how applicable it is to glaucoma follow-up.

Frequency doubling technology is an important development in perimetry. As the studies in this issue show, it is a viable screening tool. With modifications, this type of stimulus may also find a role in clinics for diagnosis and follow-up of patients with glaucoma. More studies, particularly long-term ones, are required before this technology finds its way into routine glaucoma management. Although its place in the clinic has yet to be established, its place in senior centers, shopping malls, and other screening venues seems justified.

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