Fields of OHTS: The Ocular Hypertension Treatment Study

BY CHRIS A. JOHNSON, PHD; JOHN L. KELTNER, MD; AND PAUL H. ARTES, PHD

There is a wealth of meaningful visual field data from the landmark Ocular Hypertension Treatment Study (OHTS). I asked the investigators who were most influential in designing and interpreting visual field data to break it down for us, decibel by decibel. A quick review of last issue's column by Michael A. Kass, MD, will provide an overview of the OHTS and add meaning to the findings presented herein.
—Section Editor Ronald L. Fellman, MD

WHAT WAS DISCOVERED FROM VISUAL FIELD TESTING IN THE OHTS?

The OHTS is one of the most careful and well-controlled multicenter clinical trials in glaucoma and ocular hypertension.[1-3] It is difficult to select one specific visual field finding from the OHTS that stands out from the others. We believe that there are several noteworthy findings from visual field testing in OHTS: (1) assessment of quality control, technicians' training and certification, ongoing interaction with clinical centers, and related factors associated with a visual field reading center can dramatically improve the reliability of visual fields and minimize artifactual results[4]; (2) repeated confirmation of changes in the visual field is essential to maintain high specificity and reliable interpretation of clinical visual fields[5-10]; and (3) both generalized (widespread) and localized losses in the visual field are associated with early glaucomatous visual field loss that are not related to cataract and other optical factors.[10]

IS THE FIRST REPRODUCIBLE VISUAL FIELD DEFECT IN EARLY PRIMARY OPEN-ANGLE GLAUCOMA MORE LIKELY TO BE A GENERALIZED LOSS OF SENSITIVITY OR A LOCALIZED-TYPE DEFECT?

Most patients who developed glaucoma in OHTS showed both localized as well as diffuse changes. Purely localized changes and purely diffuse changes were very rare. Localized loss, of course, is more pathognomic for glaucoma, and diffuse loss can be caused by media opacity. Clinicians should watch for both localized loss (via total- and pattern-deviation probability maps) and for diffuse change (via mean deviation [MD] and ranked-defect Bebie curves—the latter available in software such as PeriData [PeriData Software GmbH, Huerth, Germany] and the Octopus Field Analysis [Haag-Streit USA Inc., Mason, OH]). It is helpful to pay attention to the state of the crystalline lens. Diffuse changes in the visual field should not automatically be ignored, particularly if no media opacity is clinically apparent.[10]

TO WHAT SHOULD OPHTHALMOLOGISTS PAY THE MOST ATTENTION WHEN LOOKING FOR THE FIRST VISUAL FIELD DEFECT IN PRIMARY OPEN-ANGLE GLAUCOMA: ABNORMAL GLAUCOMA HEMIFIELD TEST, MEAN DEVIATION, OR PATTERN STANDARD DEVIATION?

Practitioners should primarily consider the total- and pattern-deviation probability maps when looking for early visual field loss. Glaucoma hemifield test (GHT), MD, and pattern standard deviation (PSD) are most useful when the visual field needs to be condensed into a few numbers, like when simple criteria need to be formulated. PSD is also useful with risk calculators,[11] and MD is helpful for comparing the visual fields between both eyes. Although the primary criteria for the development of visual field loss in OHTS were based on summary statistics (PSD, GHT, MD), the assessment of individual test locations was performed by the visual field readers. This was done to ensure that the localized loss of visual field was consistent with glaucoma and that confirming visual fields demonstrated losses that were reproducible in terms of the visual field location.

IF A PHYSICIAN HAS FOUR CONSECUTIVE VISUAL FIELDS DURING 2 YEARS AND IS LOOKING FOR THE FIRST SIGN OF VISUAL FIELD DAMAGE, IS HE OR SHE BETTER OFF USING A LINEAR REGRESSION ANALYSIS OR A GUIDED PROGRESSION ANALYSIS-TYPE END POINT?

Ideally, both should be used when available. Pointwise linear regression available in the Progressor (Medisoft Ltd, Leeds, United Kingdom) and PeriData softwares is more sensitive for combined focal and diffuse change (as it uses the raw sensitivity estimates), and the guided progression analysis (GPA) compensates for any diffuse change. Clinicians relying on GPA only, however, are unlikely to miss clinically significant progression if they pay careful attention to the point-by-point plots. They should beware of progression near fixation. Clinically significant changes in this region can be underrepresented by the coarse spacing of test locations. Clinicians must remember that three locations need to be changing sequentially for the GPA to warn of "likely change" or "probable change."[10]

DOES THE REDUCED REDUNDANCY THEORY OF GLAUCOMATOUS DAMAGE HAVE ANYTHING TO DO WITH THE NUMBER OF FIELDS NEEDED TO DIAGNOSE EARLY GLAUCOMA?

The concept of reduced redundancy has been introduced to account for the differences in performance (sensitivity, specificity, and other statistical measures) among various forms of visual field testing, detecting the earliest signs of functional damage, and assessing the potential mechanisms of glaucomatous loss. The number of visual fields needed to diagnose early glaucoma depends on the reliability and long-term variabil-

Gleaning the Fields of the Ocular Hypertension Treatment Study

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1. The earliest visual field defect in a patient with ocular hypertension who converts to primary open-angle glaucoma (POAG) is usually a combined form of localized and diffuse loss. It is uncommon to see only one type early on. This is important, because many ophthalmologists may only be looking for a classic arcuate defect and that would not be in the best interest of the patient with ocular hypertension. Even though arcuate defects are the hallmark of glaucoma, the Ocular Hypertension Treatment Study (OHTS) demonstrated that early on, a diffuse loss may accompany the arcuate defect or potentially diffuse loss may occur by itself in early disease.[1]

2. Localized- or arcuate-type change is best picked up by evaluating the total- and pattern-deviation plots.

3. Diffuse change is best detected be checking the mean deviation.

4. In more than 50% of patients in OHTS who developed glaucoma, the optic nerve worsened while the visual field remained normal. If you are relying mainly on the classic arcuate visual field defect to diagnose POAG, the horse is well out of the barn.

5. If you see a mild generalized loss of sensitivity in a patient with ocular hypertension, it may be the first sign of field damage. Repeat the field and re-evaluate the disc. We clinicians can no longer simply attribute generalized field loss to a nonspecific event; it could be a sign of early POAG.

6. Until we learn more, it is best to examine both longitudinal and cross-sectional visual field analyses to determine if there is a true change in sensitivity.

7. In an ocular hypertensive patient similar to those in the OHTS with initially normal visual fields, even after two reliable abnormal visual fields in a row, the next visual field was normal 36% of the time. After one abnormal visual field the next visual field was normal 85.9% of the time. However, after three abnormal visual fields, the next visual field was normal only 12% of the time. Visual fields need to be repeated several times to be sure of a definitive glaucomatous defect. Obviously, the visual field should be correlated with the disc at every visit to obtain a more meaningful picture of the overall glaucomatous process.

1. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study—a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol.* 2002;120(6):701-713.

ity of the patient. It also depends on whether the practitioner is most interested in detecting the earliest glaucomatous changes (sensitivity), the ability to correctly identify stability (specificity), the time course (rate) of changes, and other related factors.[12] A particularly useful method of evaluating the performance of visual field procedures is to use a signal-to-noise analysis. This provides a relatively parameter-free, device-independent means of determining the performance of visual field testing.[13] Additionally, clinical findings other than perimetry must be considered in conjunction with visual field results.

WHAT ARE THE MOST IMPORTANT TAKE-HOME MESSAGES REGARDING VISUAL FIELDS FROM THE OHTS?

The OHTS provided an opportunity to evaluate the importance of visual fields in the detection of glaucoma. Several key findings have emerged:

- The careful performance of visual fields can reduce errors, improve reproducibility, save time and effort, enhance consistency, and provide better quantitative information for monitoring the onset of glaucoma.
- The visual field is one of many factors associated with a diagnosis of glaucoma and must be incorporated with information about risk factors, optic disc assessment, IOP, central corneal thickness, personal and family medical and ocular history, and other clinical examination results.
- When there is uncertainty about the results of the visual field test or they appear to be suspicious for a change in function, it is best to repeat the test several times to confirm the results.
- Glaucomatous visual field loss is usually a combination of diffuse (widespread) and localized sensitivity loss.
- A glaucomatous visual field can be classified according to the shape and pattern of localized deficits to allow differentiation of glaucomatous defects from artifactual and nonglaucomatous results.
- Validated procedure for statistical analysis should be used to assess whether changes in the visual field have occurred over time.

HOW OFTEN WOULD A PHYSICIAN MISS EARLY GLAUCOMA IF HE OR SHE ONLY RELIED ON THE VISUAL FIELD FOR THE DIAGNOSIS OF PRIMARY OPEN-ANGLE GLAUCOMA?

Historically, most investigations have reported that glaucomatous changes to the optic disc are clinically noticeable more frequently than visual field losses produced by glaucoma. This was confirmed in the longitudinal OHTS, where glaucomatous changes in the optic disc were detected first in slightly more than half of the patients, even though abnormalities in the visual field were not present. In about 25% of the patients, a glaucomatous visual field abnormality appeared before changes to the optic disc, and in the other 25%, glaucomatous optic disc and visual field changes were noted at the same time.[14] In this view, it should be noted that, if only changes in the visual field (and not optic disc damage) were considered as outcome measures for this study, it is likely that it would still be continuing without a definitive result. It should also be kept in mind that technological innovations and refinements are occurring rapidly for both structural and functional losses in glaucoma, in addition to new advances in analysis and interpretation procedures.

SHOULD PHYSICIANS STILL RECOMMEND A 30-2 VISUAL FIELD, OR IS A 24-2 ADEQUATE FOR EARLY PRIMARY OPEN-ANGLE GLAUCOMA?

Most practitioners who treat glaucoma patients and individuals at risk of developing glaucoma use a 24-2 test strategy. Some reports in the literature indicate that there is no difference in the ability to detect or characterize glaucomatous visual field loss. These studies, however, were conducted using a limited number of participants, and visual field results were interspersed throughout a wide range of glaucomatous damage. Although it has not yet been published, we compared 30-2 and 24-2 visual field results for 331 superior and inferior visual field hemifields (from 184 patients) that were outside normal limits for the 30-2 test. The 24-2 visual field was created by removing the outer ring of test locations of the 30-2 pattern, except for the two extreme nasal points just above and below the horizontal meridian. Nearly 12% of the glaucomatous defects detected by the 30-2 pattern were missed (many were temporal-wedge defects), and nearly 3% of the artifactual defects noted for the 30-2 pattern (eg, droopy eyelids and trial lens rim artifacts) were judged to be glaucomatous for the 24-2 pattern. Moreover, nearly half of the patterns of glaucomatous loss of visual field were classified differently for the 30-2 versus the 24-2 test pattern. Thus, in the early stages of glaucomatous visual field loss, there may be clinically meaningful differences between the 30-2 and 24-2 test patterns. ❑

The OHTS study was supported by grants EY09341 and EY09307 from the National Eye Institute and the National Center on Minority Health and Health Disparities, National Institutes of Health, Bethesda, Maryland; an unrestricted grant from Research to Prevent Blindness, New York, New York; Merck Research Laboratories, Whitehouse Station, New Jersey; and Pfizer, Inc., Peapack, New Jersey.

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