Science and Fiction in Structure and Function

Relating the visual field and optic disc in glaucoma.

BY PAUL H. ARTES, PhD

When imaging technologies first emerged in glaucoma just over a decade ago, many of us believed that they could, in time, largely replace visual field testing in the clinical care of patients. By now, we have realized that structural and functional tests often provide complementary information and that each has its own place in the clinical care of patients with glaucoma. This article reviews some of the features of the structure/function enigma that are relevant to the question of how to integrate information from imaging and visual field examinations.

CROSS-SECTIONAL STUDIES: IMPLICATIONS FOR DIAGNOSIS

Structure/function relationships often appear curved, which has led to the popular fiction that there is a certain threshold of ganglion cell loss that must be exceeded before visual changes occur. Recent studies have shown that such nonlinearities may be statistical artifacts of scaling; they disappear when structure and function are both plotted with similar (either logarithmic or linear) units.1-5 Because contrast thresholds in a glaucomatous visual field can range over several orders of magnitude (they can vary by a factor > 3,000), logarithmic (dB) scales have become standard in perimetry.

A sensitivity loss of 3 dB with conventional perimetry is still within the statistical limits of normality (at individual test locations)6 and also within the limits of test-retest variability.7 Nonetheless, a 3-dB loss indicates a doubling of the local contrast threshold that is compatible with a 50% (3-dB) loss of ganglion cells (approximately true in the macula, although ganglion cell losses in the retinal periphery may be less severe for the same depth of visual field loss).

Current clinical measures of structural damage have similar limitations. For example, the performance of diagnostic optic disc assessments (by ophthalmoscopy, the expert evaluation of stereoscopic fundus photographs, or quantitative imaging) is limited by the enormous variation in the appearance of normal optic nerves. The statistically defined normal limit (97.5th percentile) for cup-to-disc ratio, for example, is approximately 0.7.6 A disc could have undergone massive change (say, from a cup-to-disc ratio of 0.2 to one of 0.6) but would still be classified as within normal limits. These limitations apply to many other structural variables, most of which have large normal ranges.

The described findings may help us understand why there are no simple, general rules of whether the first clinical manifestations of glaucoma occur with structural or functional tests and also why we still need to evaluate both visual fields and the optic disc in patients suspected of having early disease. Studies such as the Ocular Hypertension Treatment Study and the Structure and Function Evaluation have shown that patients with early glaucoma often display optic disc abnormalities while their standard visual field results remain within normal limits.6-11 In other patients, however, the optic disc and retinal nerve fiber layer may not reveal any hard signs of

Figure 1. Area-proportional Venn diagrams of progression with visual fields (standard automated perimetry) and the optic disc (Heidelberg Retina Tomograph [HRT]) are shown. Many patients are classified as having changed, either with visual fields or in their optic disc but not both. The overlap between visual field and optic disc progression does not improve when very stringent progression criteria are used. (Adapted from Artes and Chauhan.12)
disease despite reproducible visual field losses.

Of the 125 ocular hypertensive patients who developed overt glaucoma during follow-up in the Ocular Hypertension Treatment Study, 44 (35%) first met the study endpoint due to reproducible visual field changes. These data show that optic disc damage may not always be readily detectable before a visual field abnormality occurs.

STRUCTURE AND FUNCTION IN PROGRESSIVE GLAUCOMA

With better detection and earlier treatment of the disease, a longer life expectancy, and the call for therapies that are more tailored to each patient’s lifestyle and risk of vision loss, measuring the rate of progression will become more and more important. What roles do structure and function play in assessing progression, and how well do they agree?

The research group at Dalhousie University in Halifax, Canada, of which I am a part, recently reported longitudinal data from glaucoma patients and healthy controls who had been followed for up to 10 years. All subjects were examined twice yearly with standard perimetry, high-pass-resolution perimetry, and the HRT (Heidelberg Engineering GmbH, Dossenheim, Germany). The study used robust statistical methods to define progression, and we ensured that our criteria for change did not favor either imaging or visual field tests. One key finding was that the relationship between measures of progression with structure and function was weak. Importantly, the agreement between tests of progression did not improve when we used stricter (more conservative) criteria for change (Figure 1).

In other words, if a patient shows strong evidence of visual field progression, this change is likely to be real, no matter whether the optic disc has or has not changed during the same period. Similarly, clinicians ought not to discount evidence of changes in the optic disc because the visual field appears to be stable. The lack of concordance does not, of course, mean that the optic disc and visual field are truly independent; basic physiology demonstrates that they are not. It does mean, however, that current clinical measures of the optic disc and visual field progression, even when evaluated over a reasonably long period (7.5 years on average), are only loosely linked and therefore should be regarded as contributing complementary information to the clinical care of patients.

PROGRESSION AS A DIAGNOSTIC CRITERION

Currently, practitioners often diagnose glaucoma without the benefit of hindsight (ie, without being able to confirm change retrospectively, either on the visual field or in the retina and optic disc). The real promise of imaging tests, however, may lie in their potential to measure small changes over time (Figure 2).
Progression is the hallmark of glaucoma, and the capability of imaging technologies to measure very small structural changes makes it more feasible to use change diagnostically, particularly when following patients with ocular hypertension.\textsuperscript{13} This ability would bypass the problem of having to rely on normal limits for structural variables that have large physiological ranges. The criteria for defining change (as opposed to variability in measurements) of the visual field and the optic disc are critical and continue to evolve. Perhaps we are only just beginning to understand the meaning of structural change at the optic nerve and how to measure it. This is, after all, what makes glaucoma such an exciting field to work in at the present time.

Paul H. Artes, PhD, is at the Faculty of Life Sciences at the University of Manchester in the United Kingdom and at Dalhousie University in Halifax, Canada. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Artes may be reached at +44 0161 30 65922; paul.artes@manchester.ac.uk.