Challenges to the Common Clinical Paradigm for Diagnosis of Glaucomatous Damage With OCT and Visual Fields

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The most common clinical paradigm (CCP) for diagnosing glaucoma includes a visual field (VF) with a 6° test grid (e.g., the 24-2 or 30-2 test pattern) and an optical coherence tomography (OCT) scan of the optic disc. Furthermore, these tests are assessed based upon quantitative metrics (e.g., the pattern standard deviation [PSD] of the VF and the global retinal nerve fiber thickness of the OCT disc scan). This CCP is facing three challenges. First, the macular region (i.e., ±8° from fixation) is affected early in the glaucomatous process, and the CCP can miss and/or underestimate the damage. Second, use of the typical VF and OCT metrics underestimates the degree of agreement between structural (OCT) and functional (VF) damage. Third, resolution of the OCT scan has improved, and local glaucomatous damage can be visualized like never before. However, the clinician often does not look at the OCT scan image. Together these challenges argue for a modification of the VF test pattern and OCT protocol, replacement of metrics with a comparison of abnormal regions on VF and OCT, and careful inspection of actual OCT scan images. In principle, the CCP could be modified easily. In practice, change is facing a number of impediments.

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Many clinicians diagnose glaucoma based on the following tests: a visual field (VF) test with a 6° grid (e.g., the 24-2 or 30-2 test pattern) and an optical coherence tomography (OCT) scan of the disc, as well as photos and/or examinations of the optic disc. While disc photos typically are assessed qualitatively, in general, VF and OCT tests are compared based on objective metrics, such as the mean deviation (MD), pattern standard deviation (PSD), glaucoma hemifield test (GHT) of the 24-2/30-2 VF test grid (e.g., the 24-2 or 30-2 test pattern) and an optical coherence tomography (OCT) scan of the optic disc. Furthermore, these tests are assessed based upon quantitative metrics (e.g., the pattern standard deviation [PSD] of the VF and the global retinal nerve fiber thickness of the OCT disc scan). This CCP is facing three challenges. First, the macular region (i.e., ±8° from fixation) is affected early in the glaucomatous process, and the CCP can miss and/or underestimate the damage. Second, use of the typical VF and OCT metrics underestimates the degree of agreement between structural (OCT) and functional (VF) damage. Third, resolution of the OCT scan has improved, and local glaucomatous damage can be visualized like never before. However, the clinician often does not look at the OCT scan image. Together these challenges argue for a modification of the VF test pattern and OCT protocol, replacement of metrics with a comparison of abnormal regions on VF and OCT, and careful inspection of actual OCT scan images. In principle, the CCP could be modified easily. In practice, change is facing a number of impediments.

Second, we now have an anatomic basis for early damage to the macula. In particular, the inferior RGsCs of the macula (i.e., those associated with the superior VF defects near fixation), enter the highly vulnerable inferior quadrant.1,2,18 Of note, only 2 of the 24-2/30-2 VF test locations fall within this highly vulnerable region of the VF, which is only approximately 2% of the retinal area, but includes over 30% of the retinal ganglion cells (RGC).3 This region is vital for everyday visual tasks, such as reading, driving, and recognizing faces.4–6 Four recent lines of evidence question the efficacy of the CCP in detecting glaucomatous damage to the macula. First, glaucomatous defects near fixation are missed and/or underestimated with the 24-2/30-2 VF.7–11 For example, in a recent study,12 the commonly used criteria of an abnormal PSD and/or GHT on the 24-2 VF test missed 13 (22.8%) of 57 glaucomatous eyes, and 11 of these 13 had macular damage. Interestingly, early static perimetry, and even earlier Goldmann perimetry, studies showed examples of eyes with glaucomatous damage near fixation.7,14–17 More to the point, one early study17 suggested that damage occurred first in the macula, and a second7 that this damage was missed by a 30-2 test pattern.7 However, until recently, this work was largely ignored as evidenced by the paucity of references to these studies, and the lack of impact on the CCP. In part, this is due to a belief that the axons from the macular RGsCs entered the relatively less vulnerable region of the optic disc, the temporal quadrant, and, thus, are the last to be affected by glaucoma. This resulted in a generally held belief that the 10-2 is useful only in the case of advanced glaucoma or threat to fixation.

Third, early macular damage is missed and/or underestimated by the OCT disc scan of the CCP, especially if metrics, such as global, quadrant, or clock-hour cpRNFL thickness and probabilities, are used.19 Interestingly, other early OCT studies20–21 also suggested macular damage was common, and these also had little impact on the CCP. Finally, the fourth line of evidence is that early diffuse damage due to glaucoma also can affect the macula, and the OCT disc scan of the CCP can miss this damage as well.22

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Challenge 2: Structural (OCT) and Functional (VF) Damage Typically Agree, and VF and OCT Metrics are a Poor Way to Assess This Agreement

The second challenge comes from an improved understanding of the relationship between functional damage, as seen on VFs, and structural damage, as seen on OCT scans. While it commonly is assumed that structural damage precedes functional damage, the actual situation is more complex. In particular, the extent to which structural damage appears before functional damage depends upon the test performed (e.g., OCT macular vs. disc scans; 24-2 vs. 10-2 VFs) and the metrics used (e.g., VF GHT vs. PSD vs. MD vs. cluster criteria), as well as their measurement error. It also depends upon the level of cpRNFL thickness and 24-2/30-2 visual sensitivity of the patient when healthy (i.e., before glaucoma develops). Structural damage often will be detected before functional damage when using the 24-2/30-2 VF OCT disc scan, and standard metrics. However, these metrics miss clear damage seen by comparing abnormal regions on VF and OCT probability maps. That is, the CCP does not make full use of the information available to us from either VF or OCT testing.

Implications for the CCP

These two challenges suggest that radical changes should be made to the CCP. First, scans that include the macula and disc are necessary so that macular RGC and RNFL thickness can be assessed, in addition to the typical measure of the cpRNFL thickness around the disc. The scan protocol can be a single scan that includes the macula and disc or two separate cube scans, one centered on the fovea and one on the disc. The resulting RGC and RNFL thickness maps should be turned into probability/deviation maps to facilitate comparison with VFs. Second, VFs should be obtained with a pattern that includes a finer test grid in the macular area or 24-2 and 10-2 tests should be performed within the first two visits. Finally, instead of conventional metrics, VF and OCT results should be compared topographically. That is, abnormal points seen on VFs should agree topographically with the local abnormal regions on RGC and RNFL probability maps, and this region of agreement should resemble known patterns of glaucomatous damage.

We have designed a one-page report that incorporates these suggestions. Two OCT manufacturers are incorporating the basic elements of these suggestions in a new report, and a third has a report that has some of these elements.
Damage. For example, Figure 1D shows the temporal half of the papillary images, such as in Figure 1C, and this can help the clinician interpret the scan and, more importantly, the quality of the software's circumpapillary image. The clinician can assess the quality of this scan and, more importantly, the quality of the software's circumpapillary image. The improvement that has occurred in the quality of the OCT images provides a third challenge to the CCP, as well as providing the opportunity to improve our understanding and diagnosis of glaucoma. Retina specialists routinely look at the b-scans of OCT images, while glaucoma specialists typically do not. Why? The answer is simply, "because we never did." That is, early time-domain OCT reports were based upon averaged circle (Fig. 1A) scans and the circumpapillary image presented was too small to be of use, which was understandable given the quality of the time-domain OCT instrument for a healthy eye. Compare the quality of this image to that of a typical spectral domain image in Figure 1C, which is from an eye with glaucomatous damage. Circumpapillary images of this quality have been available for 8 years or so. However, most recent OCT glaucoma reports still show OCT circumpapillary images that are too small to be of use, and some recent reports do not show any OCT images.

Why look at the actual scan images? First, by examining the circumpapillary image, the clinician can assess the quality of the scan and, more importantly, the quality of the software's automated delineation (segmentation) of the borders of the RNFL. Second, an OCT scan through the fovea often will reveal nonglaucomatous damage due to age-related macular degeneration, epiretinal membrane, macular edema, holes, and so forth. Finally, local details of damage can be seen on circumpapillary images, such as in Figure 1C, and this can help the clinician understand and follow changes in glaucomatous damage. For example, Figure 1D shows the temporal half of the image in Figure 1C compared to the adaptive optics scanning laser ophthalmoscopy images for the same locations. Local damage clearly is visible on the OCT image.

**Implications for CCP**

OCT scans have approximately 100 times the resolution of a magnetic resonance imaging (MRI) scan. We would not trust a computer algorithm to follow a tumor in the brain without a radiologist actually looking at the scan. At the very least, clinicians routinely should scrutinize an enlarged image associated with a circle around the disc. Preferably this image would be obtained from an averaged circle scan, although for most purposes it could be derived from OCT cube scans that include the optic disc. Also, we advise examining a scan through the fovea for the reasons mentioned above. In addition, contrary to commonly held beliefs, examination of scan images allows one to study eyes with high myopia or advanced glaucoma. Let us consider the latter first.

It is generally held that OCT is not suitable for following severe glaucoma, defined as a 24-2 MD worse than −15 dB. It is true that regional (i.e., clock hours or quadrants) and global cpRNFL thickness approaches an asymptotic thickness, or floor, for a population of eyes with MD ≤ −15 dB. While this suggests that you cannot use the global cpRNFL thickness to follow these eyes, it does not mean that you cannot use the OCT. In fact, if a small portion of the VF is remaining, you will see a relatively preserved region of cpRNFL matching that location on the VF. This is illustrated in Figure 2, where the 24-2 VF shows a region of preservation. There is a corresponding region of preserved cpRNFL on the circumpapillary scan in Figure 2B, which can be followed to assess progression.

It is also generally held that OCT is not suitable for studying high myopes, because metrics, such as global cpRNFL thickness, depend upon a normative database that excludes eyes worse than ±6 diopters. Again, examination of the actual circumpapillary image typically will allow for an assessment of glaucomatous damage, as well as allow one to follow this damage for progression.

**Are We in the Middle of a Paradigm Shift?**

There is some evidence that the CCP is (very) slowly changing. Compared to 5 years ago, more clinicians are obtaining 10-2 VFs and OCT macular scans to assess early glaucomatous damage. However, most clinicians still depend largely upon 24-2 VFs and OCT disc scans, and relatively few look at the functional test or the OCT disc scan as our only structural test. These tests do not optimally measure glaucomatous damage. Further, we would not be using metrics to assess VF or OCT abnormalities, or to compare these tests, although artificial intelligence may help. Finally, given that clinical fundus exams are routine and many OCT machines provide optic disc images, there is even some chance that fundus photographs would be unnecessary (or performed less frequently), especially with improved OCT disc analysis.

In sum, the CCP is suboptimal for understanding, diagnosing, and following glaucomatous damage. In principle, this can be changed easily. In practice, it faces a number of impediments, including the current "clinical standard of care," the long-standing views of opinion leaders, the software available in VF and OCT instruments, government mandated billing practices, and even the order of tests done at some clinics. However, none of these challenges is evidence-based; they exist for the simple reason that this is the way we have always done it.

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