WHERE DOES GANGLION CELL ANALYSIS FIT?

The role of macular optical coherence tomography in glaucoma assessment.

BY HIROSHI ISHIKAWA, MD

Optical coherence tomography (OCT) has become a staple in noninvasive imaging for ophthalmology. This strategy provides quantitative as well as qualitative clinical measures/information for various ocular pathologies.[1-4] With spectral-domain OCT technology, which has a higher scanning speed and improved axial resolution compared to time-domain OCT, it is possible to perform 3-D volumetric scans of the retina and obtain detailed retinal layer analysis in an objective and reproducible fashion.[5-8]

The circumpapillary retinal nerve fiber layer (cpRNFL) thickness measurement has become a well-established and widely used biomarker in glaucoma assessment since the introduction of OCT.[9-11] In addition to excellent glaucoma discriminating performance, cpRNFL may offer equivalent performance in glaucoma progression assessment, but this statement remains the subject of debate.[12-17] As it measures the thickness along a circle close to the optic nerve head (ONH) margin, cpRNFL covers all the axons of the ganglion cell distributed in the entire retina, but it is not a direct measurement of the glaucoma insult to retinal ganglion cells (RGCs). Instead, cpRNFL is an indirect measure of the consequence of the ganglion cell body damage (the controversy surrounding this statement is along the lines of the debate over which came first, the chicken or the egg).

With its higher resolution and denser sampling of spectral-domain OCT, ganglion cell analysis has become a reality.[18-20] As a result, two new OCT parameters for glaucoma assessment have been introduced: ganglion cell inner plexiform layer (GCIPL) and ganglion cell complex (GCC) thickness. Neither is a pure ganglion cell layer analysis, however, because it is difficult to segment the border between ganglion cell and inner plexiform layers. These two layers are thus combined together as GCIPL to reduce the inaccuracy of automated layer segmentation. GCC goes one step further by including macular RNFL on top of the GCIPL. Because all inner retinal layer borders are generally harder to segment in a precise and reproducible way than inner limiting membrane and retinal pigment epithelium, combining multiple layers improves the stability (or reproducibility) of segmentation performance; at the same time, however, it may reduce sensitivity to glaucomatous damage by including a structure that is not the primary site of glaucomatous damage, namely the inner plexiform layer.[18]

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IS GANGLION CELL ANALYSIS BETTER THAN CONVENTIONAL cpRNFL?

The macular region contains a high concentration of more than 50% of RGCs, which can be quantified relatively easily compared to peripheral RGCs that may be too thin for OCT to measure reliably.[21-23] In addition, the macular region is the primary location of glaucomatous damage in the disease's early stage. It therefore makes sense to measure RGCs in the macular region. On the other hand, unlike the cpRNFL that covers the entirety of RGC axons, current ganglion cell analysis ignores close to 50% of RGCs outside the macular region, representing the strategy's major weak point.

Many published studies have investigated GCC and/or GCIPL performance in glaucoma assessment compared with the cpRNFL.[19,23-26] In brief, they are both equally effective for diagnosing glaucoma and assessing its progression. Some studies took a different perspective and combined ganglion cell analysis with conventional cpRNFL and optic disc analysis instead of comparing their performance.[27-30] These researchers found that combining structural measurements improved glaucoma assessment performances more than using them separately, but currently, no one definitive index illustrates the magnitude of glaucomatous damage that is

AT A GLANCE

- Ganglion cell analysis with optical coherence tomography provides nearly equivalent glaucoma assessment performance as conventional circumpapillary retinal nerve fiber layer thickness measurement.
- Combining ganglion cell analysis with circumpapillary retinal nerve fiber layer thickness measurement may provide a better biomarker for glaucoma management.
- Because of the technical advantages of macular scans with optical coherence tomography, performing both macular and optic nerve head scans in cases of glaucoma is recommended.

automatically calculated based on all available structural measurements. The question then becomes, how does the ganglion cell analysis fit into daily clinical tasks? The answer lies in the OCT image acquisition technique.

ADVANTAGES OF OCT MACULAR SCANS

The macular region is the easiest location to perform OCT imaging, because the optical axis of the eye is naturally aligned to the foveola. Conventional cpRNFL requires an ONH scan, which needs an optical path shifted from the optimal central path. In addition, patients are instructed to look at a fixation target that deviates from the natural center, which places additional tension and strain on the eye. All of these things affect OCT signal quality. In my experience as the director of the Ocular Imaging Center at UPMC Eye Center, there is a consistent trend of better OCT signal quality with macular scans than ONH scans, especially in elderly and diseased eyes.

It is obviously ideal to perform both macular and ONH scans for glaucoma assessment when possible. In worst-case scenarios, however, clinicians should prioritize macular scans, because the ganglion cell analysis provides equivalent glaucoma assessment performance, more or less, as the cpRNFL. At UPMC, therefore, all glaucoma patients undergo macular scans first, then ONH scans.

CONCLUSION

Ganglion cell analysis can serve as an alternative OCT structural assessment when ONH scans are difficult. It is better to use both ganglion cell analysis and the conventional OCT measurements as complements to each other, however, in order to make a comprehensive glaucoma assessment. ■

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