Editorial

Macular segmentation in Neuro-Ophthalmology: Descriptive or predictive?*  
¿Segmentación macular en Neuro-Oftalmología: descriptiva o predictiva?  
G. Rebolleda*, F.J. Muñoz Negrete  
Servicio de Oftalmología, IRYCIS, Hospital Ramón y Cajal, Madrid, Spain

Examining the macula by means of segmentation with optic coherence tomography (OCT) has expanded our analytical capacity when compared with the conventional examination of the peripapillary retina nervous fiber layer (RNFL), to the extent that at present, in addition to evaluating macular axons (macular nervous fiber layer), we are able to evaluate the neuronal sub-populations comprising said layer (ganglion cell layer, internal and external nuclear layer).1  

Version 6.0 of OCT-Cirrus (Carl Zeiss Meditec, Dublin, CA, USA) enables the quantification of the joint thickness of the ganglion cell and internal plexiform layers (GCL/IPL) by means of a 6 mm × 6 mm Q which contains an electric ring centered on the macula. This provides the thickness of 6 sectors (3 upper and 3 lower) and 2 overall values (average and minimum). It also includes a database that facilitates the interpretation of obtained results with the additional advantage of analyzing macular explorations carried out with previous versions of the device.  

The distribution of ganglion cells in the macula is more regular and has less variation between individuals than the peripapillary RNFL, linked to anatomic optic disk variations, with excellent reproducibility2 and therefore lower incidence of false positives.  

In the context of patients with multiple sclerosis (MS) with and without optic neuritis it has been demonstrated that, in addition to the well known significant loss of peripapillary RNFL, there is a significant thinning of the macular RNFL and the GCL/IPL when compared to healthy subjects. In addition, the correlation of the damages found in the examination of ganglion cells with visual function (visual acuity and contrast sensitivity) as well as with the degree of neurological disability (EDSS) is higher than that observed with damaged peripapillary RNFL. In other words, the GCL/IPL thickness has a better structure–function correlation than the examination of the papillary RNFL in patients with MS.  

GCL/IPL has been observed in all MS subtypes but is more marked in the progressive secondary form when compared with the remitting-recurring form. But regardless of the subtype, damage is more acute, as was observed with RNFL in eyes with optic neuritis history.3,4,5  

In addition, a good correlation has also been observed with magnetic resonance (MR) findings both in what concerns overall volume and white and gray substances.6,7,8  

In our experience the diagnostic capacity of GCL/IPL is greater than peripapillary RNFL analysis because it detects clinical and subclinical damages in approximately half of all patients, and in about 70% of patients with optic neuritis history.  

Macular segmentation has enabled the definition of a new phenotype of patients with MS where thinning of the macula as well as of the internal and external nuclear layers can be observed with normal RNFL analysis. This group of patients exhibits higher neurological deterioration9 which suggests primary neuron damage and supports previous postmortem

* Corresponding author.  
E-mail addresses: grebolleda@telefonica.net, francisco.munoz@uah.es (G. Rebolleda).

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histological findings in patients with MS where, in addition to axon death, cell death was observed in various levels of the retina (primary retinal neuropathy).10

Recently, Gelfand et al.11 have described in 15 of 318 patients (4.8%) with MS a microcystic macular edema mainly located at the level of the internal nuclear layer which was not present in any healthy subjects and could be a sign of an inflammatory condition preceding neuron death and therefore thinning. On the other hand, it could be a sign of the damage mechanism which is unrelated to the demyelinating episode. Affected patients exhibited greater neurological deterioration which indicates that it could be related to greater severity of the disease.

In a very recent study, Saidha et al.12 found that the microcystic edema or the thickness of the internal nuclear layer observed in patients with MS has prognostic implications, i.e., rates of thickness or the presence of edema are significantly associated with the development of new lesions in MR, an increased number of recurrences and greater neurological deterioration. If in subsequent studies the association of internal nuclear layer thickening or the presence of edema with the activity of the disease can be confirmed, the thickness of the internal nuclear layer could be considered as a prognostic marker in patients with MS. This potential predictive role is supported by the fact that said thickening is significantly larger in patients with optic neuritis than in patients with MS.13

Turning now to our recent experience with the analysis of GCL/IPL in the macula, it has allowed us to infer the existence or absence of neuronal death in the acute phase in patients with optic neuropathy and papillary edema. This is an extraordinarily valuable piece of data because of the damage in the peripapillary RNFL is masked by the edema. This finding could be applicable to any neuropathy with papillary edema (ischemic optic neuropathy, papillitis, papiledema, dysthyroid or compressive neuropathy, etc.), provided that there is no associated macular pathology or edema which could obviously interfere with the segmentation or interpretation of data.

In a preliminary unpublished study in progress we have been able to demonstrate that in papilledema the study of macular ganglion cells plays a particularly relevant role, which means that a normal analysis of GCL/IPL would have favorable prognostic implications while the presence of thinning would involve irreversible structural damage thus pointing to more aggressive therapeutic approaches. This finding is even more relevant if, as discussed above, we take into account that the peripapillary examination in the papillary edema phase masks the damage that could be occurring and, the more acute the damage, the greater the relevance of the finding.

We have also observed that about 15% of patients with pseudoeidema due to optic nerve hidden drusen exhibit GCL/IPL thinning at the macular level which goes unnoticed with conventional RNFL analysis.

In summary, in patients with MS, GCL/IPL examination is more sensitive and is better correlated with visual and neurological deterioration as well as with neuroimaging findings. On the other hand, internal nuclear layer thickening as a potential prognostic indicator opens up a new pathway of study and, together with the analysis of the remainder of subpopulations, will allow us to sequence and locate the site where the primary damage occurs.

GCL/IPL examination in the presence of papillary edema offers a unique opportunity to infer damages before they occur. In addition, in the specific case of papiledema, these data could be crucial for our therapeutic approach both at diagnosis and during follow-up.

REFERENCES


