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5-2019

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### Repository Citation

Sudhakar, Padmaja, "Commentary: Ganglion Cell Complex of Retinal Layer Thickness by Optical Coherence Tomography in Cases of Multiple Sclerosis without Optic Neuritis Compared to Healthy Eyes" (2019). *Neurology Faculty Publications*. 57.  
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## Commentary: Ganglion Cell Complex of Retinal Layer Thickness by Optical Coherence Tomography in Cases of Multiple Sclerosis without Optic Neuritis Compared to Healthy Eyes

Digital Object Identifier (DOI)

[https://doi.org/10.4103/ijo.IJO\\_175\\_19](https://doi.org/10.4103/ijo.IJO_175_19)

### Notes/Citation Information

Published in *Indian Journal of Ophthalmology*, v. 67, issue 5.

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## Commentary: Ganglion cell complex of retinal layer thickness by optical coherence tomography in cases of multiple sclerosis without optic neuritis compared to healthy eyes

Peripapillary retinal nerve fiber layer (pRNFL) thickness can be non-invasively measured by optical coherence tomography (OCT). This has been considered as a strong biomarker of axonal degeneration in multiple sclerosis (MS). This testing is also relatively inexpensive and less time consuming compared to magnetic resonance imaging. With increase in the number of disease modifying therapies for MS OCT can serve as a good biomarker to describe the stability or progression of the disease.

On an average it is believed that pRNFL decreases by 1-2  $\mu\text{m}$  per year in MS according to some studies.<sup>[1,2]</sup> Also the pRNFL has been shown to be thinner in progressive MS compared to stable relapsing remitting MS.<sup>[3]</sup> Optic neuritis in MS can lead to pRNFL thinning a few months later due to retrograde axonal degeneration and/or trans-synaptic degeneration.<sup>[4,5]</sup> However, the pathophysiology underlying pRNFL thinning in MS without optic neuritis is not entirely understood. This might suggest an ongoing neurodegenerative process.<sup>[3]</sup> Achievement of no evident disease activity with disease-modifying treatment in MS has been associated with less marked atrophy of the pRNFL longitudinally.

The previous time domain OCT-based studies in MS also demonstrated that there is atrophy of the pRNFL. With the spectral domain OCT that has a much higher resolution, automated segmentation of the individual retinal layers and analysis of their thickness is possible. Five of the 10 retinal layers have been analyzed systematically in MS besides the RNFL: Ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), and outer nuclear layer (ONL).

According to a meta analysis<sup>[6]</sup> that studied the retinal layer segmentation in MS, pRNFL thinning was seen in multiple sclerosis with optic neuritis (MSON) (mean difference  $-20.10 \mu\text{m}$ , 95% CI, range  $-22.76$  to  $-17.44$ ;  $P < 0.0001$ ) and in multiple sclerosis without optic neuritis (MSNON) (mean difference  $-7.41 \mu\text{m}$ , range  $-8.98$  to  $-5.83$ ;  $P < 0.0001$ ) compared to controls. In contrast, the present manuscript that studied MS without optic neuritis in ARAB patients found no difference in the pRNFL in MSNON and control subjects. However, the authors already identified the limitations of this study as it was a cross sectional, and thus a longitudinal study may be necessary for assessment.

The meta analysis<sup>[6]</sup> also demonstrated that besides the pRNFL, macular RNFL also showed thinning of  $-6.18 \mu\text{m}$  (range  $-8.07$  to  $-4.28$ ;  $P < 0.0001$ ) in MSON eyes and thinning of  $-2.15 \mu\text{m}$  (range  $-3.15$  to  $-1.15$ ;  $P < 0.0001$ ) in MSNON eyes compared to controls. Similarly, the present manuscript has also noted macular RNFL thinning in MSNON eyes compared to controls. They additionally looked at superior and inferior macular thinning individually in MSNON and felt that both were thinner compared to controls.

Macular ganglion cell layer and inner plexiform layer (GCIPL) atrophy was described in the meta analysis<sup>[6]</sup> for MSON eyes ( $-16.42 \mu\text{m}$ ) and MSNON eyes ( $-6.31 \mu\text{m}$ ) compared to controls. This manuscript also showed that the mean thickness of the macular GCIPL (described as ganglion cell complex GCIPL) was thinner in MSNON compared to controls. Also interestingly, the mean ganglion cell complex (GCIPL) and total GCL++ thickness (thickness of GCL + IPL + nerve fiber layer) in the superior macula in MSNON group was thinner than the control group. Hence, superior macula seems most affected in MSNON as per this manuscript.

Atrophy of retinal layers in MS stops at the inner nuclear layer.<sup>[6]</sup> Consequently, volume changes of the INL have emerged as a potentially new surrogate for inflammation-related changes in MS and also for studying response to immune therapy.<sup>[7]</sup> The degree of inner retinal layer (RNFL, GCIPL) atrophy is most marked in the early disease course. This finding has also been reflected in the present study.

Most of the published data have described the OCT findings seen in western MS population. However with MS now being prevalent in the Gulf countries, this manuscript has served an important purpose of describing OCT findings in the non-western population. Most of it correlates with that described in western MS patients.

Therefore with all the available evidence, it is apparent that OCT should be included as a routine procedure in monitoring MS. It serves several purposes such as monitoring for neurodegeneration,<sup>[2,8]</sup> for distinguishing progressive from stable relapsing remitting MS and also for studying response to disease modifying therapy longitudinally.

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<b>Quick Response Code:</b>	<b>Website:</b> www.ijo.in
	<b>DOI:</b> 10.4103/ijo.IJO_175_19

**Cite this article as:** Sudhakar P. Commentary: Ganglion cell complex of retinal layer thickness by optical coherence tomography in cases of multiple sclerosis without optic neuritis compared to healthy eyes. *Indian J Ophthalmol* 2019;67:653-4.