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Neuro-ophthalmology Update

OCT: New perspectives in neuro-ophthalmology

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Abstract

Optical coherence tomography (OCT) has become essential to evaluate axonal/neuronal integrity, to assess disease progression in the afferent visual pathway and to predict visual recovery after surgery in compressive optic neuropathies. Besides that OCT testing is considered a powerful biomarker of neurodegeneration and a promising outcome measure for neuroprotective trials in multiple sclerosis (MS).

Currently, spectral-domain OCT (SD-OCT) technology allows quantification of retinal individual layers. The Ganglion Cell layer (GCL) investigation has become one of the most useful tools from a neuro-ophthalmic perspective. It has a high correlation with perimetry, is predictive of future progression and is a highly sensitive, specific of several neuro-ophthalmic pathologies. Moreover the superior correlation with clinical measures compared to peripapillary retinal nerve fiber layer (pRNFL) suggests that GCL analysis might be a better approach to examine MS neurodegeneration.

In disorders with optic disk edema, such as ischemic optic neuropathy, papillitis and papilledema, reduction in RNFL thickness caused by axonal atrophy is difficult to distinguish from a swelling resolution. In this setting, and in buried optic nerve head drusen (ONHD), GCL analysis may provide more accurate information than RNFL analysis and it might be an early structural indicator of irreversible neuronal loss.

Enhanced depth imaging OCT (EDI-OCT) provides *in vivo* detail of ONHD, allowing to evaluate and quantify the drusen dimensions.

OCT is improving our knowledge in hereditary optic neuropathies. Furthermore, there is growing evidence about the role of OCT as an adjunctive biomarker of disorders such as Alzheimer and Parkinson's disease.

Keywords: Neuro-ophthalmology, Optical coherence tomography, Ganglion cell layer

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Introduction

Optical coherence tomography (OCT) has revolutionized ophthalmology and it has become one of the most important tools in neuro-ophthalmic practice.

Time-domain OCT (TD-OCT) was widely used in clinical practice and currently replaced by the newer Spectral-Domain OCT (SD-OCT) technology that offers considerable improvements. SD-OCT has faster acquisition time and higher resolution than TD-OCT, providing high quality three dimensional images. Furthermore it can track eye movements and it has eliminated operator bias with automatic centering.

OCT is a quick, sensitive, non-invasive, user-friendly device that provides high-resolution images of the peripapillary retinal nerve fiber layer (pRNFL), macular volume, macular ganglion cell layer (GCL), and optic nerve head, yielding

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reproducible and reliable measurements. OCT allows us to search about axonal-neuronal integrity in the afferent visual pathway and, compared with perimetry, is faster, more reproducible, precise and less dependent on patient.

Depending on the type of disorder, OCT provides data relevant for diagnosis, follow-up, and prognosis. Although diagnosis exclusively based on OCT is not possible, in some diseases there are pathognomonic findings leading to correct diagnosis. This review gives an overview on current applications, typical changes, new perspectives and future directions of the OCT in the following diseases: optic neuritis (isolated or associated with multiple sclerosis or neuromyelitis optica), anterior ischemic optic neuropathy, papilledema, optic nerve head drusen, autosomal dominant optic atrophy, Leber hereditary optic neuropathy and neurodegenerative diseases.

Optic neuritis/multiple sclerosis

Multiple sclerosis (MS) is a disorder characterized by inflammation and neuro-axonal degeneration. Optic neuritis (ON) is one of the manifestations of MS and is the presenting event in 25–50% of MS cases. Given its high degree of reliability, sensitivity and ease of use, OCT is an ideal method for assessing pathologic changes in the anterior visual pathway of patients with ON and MS.

Retinal nerve fiber layer thickness

Firstly reported by Parisi in 1999, thinning of pRNFL by OCT, is a well-documented structural marker of axonal degeneration in MS, which occurs even in the absence of optic neuritis (ON).[1–6]

OCT confirms the presence of optic disk edema in anterior ON, and quantifies the severity of axonal loss that follows the acute episode. OCT can detect subclinical axonal loss in eyes with normal visual fields and normal visual acuity (Figs. 1 and 3).[7]

Meta-analyses of data for TD-OCT show that RNFL thinning is milder in MS without ON (7.08 μm) than in eyes that have suffered ON (20.38 μm) and it is more pronounced in the temporal quadrant.[4]

Rebolleda et al. demonstrated by OCT an enlarged cup to disk ratio after unilateral ON that correlated with RNFL thinning (Fig. 2). A cupping asymmetry equal or greater than 0.2 was present in around 25% of cases.[8]

RNFL thickness correlates with visual and neurological functioning as well as with paraclinical data and disease duration. The strongest correlations were shown in studies including patients with MS and ON antecedent.[3,4,9]

A moderate association has also been shown between the RNFL thickness and several magnetic resonance imaging (MRI) findings characteristic of brain atrophy.[3,10] A strong correlation with MRI results is unlikely since axons are not the only component of the brain and brain atrophy also reflects loss of myelin, gliosis, synaptic and water content changes.

Studies using newer SD-OCT corroborate previous findings by TD-OCT, where RNFL thinning typically occurs in the temporal quadrant,[5,11–13] although measurement values cannot be directly compared and there is also a substantial color-code disagreement among SD-OCT devices (Fig. 1).[13,14]

Spectralis-OCT incorporated the N-site axonal protocol which differs from the standard pRNFL scan because it starts and terminates in the nasal side of the optic nerve, focusing on the temporal quadrant. Using this protocol in patients with remitting-relapsing MS (RRMS), Spectralis yields a significantly higher thinning for the temporal quadrant than OCT Cirrus in non-ON eyes, suggesting that N-site axonal analysis could define axonal damage earlier than conventional RNFL analysis.[5]

Macular and Ganglion cell layer thickness

Initially, OCT focused primarily on the evaluation of pRNFL. The latest OCT investigations involve segmentation of specific retinal layers allowing quantification of both axonal damage (RNFL) and neuronal degeneration. Several studies have shown that patients with RRMS exhibit a significant thinning of both, pRNFL and ganglion cell layer (GCL),[15–19] and the damage is more pronounced in eyes with ON antecedent (Fig. 1).

OCT-GCL thickness analysis is more sensitive to detect damage and is reduced before than pRNFL analysis in RRMS patients, even in the absence of a previous episode of ON.[18,19] Unsurprisingly, the sectors showing the highest abnormality rate in GCL analysis are the supero and inferonasal (Fig. 3).[20] Moreover, macular GCL thickness correlates better with visual dysfunction [visual acuity (VA), low-contrast letter acuity, and vision-specific quality of life measures, visual field mean deviation (MD)], disability and MRI than RNFL thickness.[15,18]

The improved reproducibility of SD-OCT enhances the value of the analyzed data from individual quadrants in the longitudinal evaluation of MS patients.[21,22] Progressive RNFL and ganglion cell inner plexiform layer (GCIPL) thinning occurs as a function of time in patients with MS, even in the absence of ON, and is associated with clinically significant visual loss.[23–27] Narayanan reported that RNFL and GCIPL decreased with follow-up time by −1.49 and −0.53 μm/year, respectively.[25] Progressive changes seem to correlate with changes in neurological impairment measured by the Expanded Disability Status Scale (EDSS).

Macular edema and MS

SD-OCT has become the most useful tool for the diagnosis of macular edema that could appear in MS patients with intermediate uveitis or as a side effect of Fingolimod (FTY-720). A review of clinical trials reported that Fingolimod 0.5 mg and 1.25 mg were associated with a low incidence of macular edema (0.3% and 1.2%, respectively) that is a dose-dependent adverse event and typically resolves upon cessation of therapy. An ophthalmic examination before initiating fingolimod therapy and regular follow-up eye examinations by OCT during therapy are recommended.[28]

In 2012, Gelfand et al.[29] identified by OCT a microcystic macular edema (MME) in patients with demyelinating optic neuropathy. MME is characterized by small hyporeflective spaces within the inner nuclear layer (INL) in the parafoveal region of the retina. In microvacuolar aspect, the sparing of fovea and the limitation to the INL distinguish MME from other macular edemas caused by vascular leakage (Fig. 4).