What Does Optical Coherence Tomography Offer for Evaluating Physical Disability in Patients with Multiple Sclerosis?

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ABSTRACT

Visual dysfunction is one of the most common clinical manifestations of multiple sclerosis (MS). For example, optic neuritis is the onset symptom in 20% of patients with MS. Visual pathway impairment presents in most patients with MS, including patients who have not experienced optic neuritis. During the last decade, many clinical trials of MS have included visual outcomes. One tool used in these studies, optical coherence tomography, is a non-contact, noninvasive, high-resolution optical imaging technology that helps segmentation and measurement of

specific retinal layers using computerized algorithms. Optical coherence tomography is used in various stages of MS from diagnosis to treatment of the disease. In this review, we summarize the use of optical coherence tomography in MS and study its usefulness for evaluating the physical disabilities of MS patients.

Keywords: Ganglion cell layer, inner plexiform layer, multiple sclerosis, physical disability, optical coherence tomography, retinal nerve fiber layer

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OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) is a non-contact, noninvasive, high-resolution optical imaging technology, in light of impedance between a signal from an object under observation and a signal from another object used as a local reference (1-3). OCT is an optic analogue of standard ultrasound, which technically relies on the reflection of high-frequency sound waves with a limited resolution of around 150 µm. Interestingly, OCT utilizes the reflection of short wavelength light (usually a wavelength of 830 nm), resulting in a resolution of 10 µm (1, 2).

OCT is a Michelson interferometer based technology, that processes A-scan signals from interference patterns produced from a low coherence light reflection from tissues and a reference mirror. An Image is formed, when, multiple A-scan signals are aligned, which can somewhat be seen as an in-vivo histology. In the course of the most recent decade, OCT innovation has extended from its former time-domain (TD) model to the later, spectral-domain (SD) model. TD-OCT examines the time difference between the reflection of light from the tissue assess depth—and a control echo from a portable reference mirror. Whereas SD-OCT depends on the mathematical Fourier transformation equation and displaces with the requirement for a reference mirror which, therefore, makes It a component of various light wavelengths instead of time echo delays. Therefore, it is faster and gives a better image quality (5 µm versus 10 µm) than its antecedent. Moreover, the faster the scanning speed, the more data to be obtained in shorter timeframes. In this way, SD-OCT allows three dimensional imaging of the retina as opposed to the two dimensions accessible in TD-OCT (1, 2, 4-6).

OCT has advanced over the past 10 years to a standout amongst the most essential ancillary tests in ophthalmic practice. It has so far, enabled a high-resolution, cross-sectional imaging of the cornea, irido-corneal angle, retinal nerve fiber layer (RNFL), macular region, ganglion cell layer, and optic nerve head. In this way, OCT has been in use for the past ten years in assessing front and back ocular pathologies as a major aspect of routine ophthalmic examinations. The OCT is useful in many ways, including, gaining insight into brain damage issues in various central nervous system disorder through observation of the axonal-neuronal integrity in the front part of the afferent visual pathway (7-9).

The frontal visual pathways comprise of the retinal ganglion cells (GC). Their somas are in the ganglion cell layer (GCL). Their axons shape the RNFL and are unmyelinated until the point that they wind up myelinated inside the optic nerve, where they form a white matter tract. These axons frame the optic nerve, which voyages by means of the optic trench to the optic chiasm. The nerve filaments on the nasal sides of every retina traverse (decussate) in the optic chiasm, and the greater part of the strands at that point go ahead to neurotransmitter at the parallel geniculate core (1, 2, 5).

MS is defined by both inflammation and deterioration of axons. Symptoms are visible with most MS patients. In about 20% of MS patients, appearance of symptoms begins with Optic neuritis (ON) first. With or without undergoing ON, 90% patients have a higher tendency of developing lesions in their pathways irrespective of ON history, as shown

in post-mortem (10–12). Reduction in the thicknesses of the RNFL and the ganglion cells/inner plexiform layer (GCIPL) in MS patients –both whether they underwent ON or not– have been shown in many studies. However, the pathological mechanism is yet to be known. Some speculations about RNFL and GCIPL thickness reduction relays inflammation or vasculitis; trans-synaptic deterioration; lesions in the optic radiation; retrograde degeneration after ON; retrograde degeneration after a mild, subclinical ON; and basic deterioration of the GCIPL neurons as a result of MS (8–12).

Optical coherence tomography and MS

OCT is utilized in different phases of MS from diagnosis to treatment of the disease (13–27).

1. Evaluating visual function: Visual disability is in connection with OCT parameters in MS whether they underwent ON or not (13–15).
2. Differential diagnosis of ON and MS disorder: RNFL thickness increases in acute ON and decreases in chronic ON. Regarding neuromyelitis optica spectrum disease, the depletion in GCIPL and RNFL thicknesses tends to be more serious than in MS-associated ON. In Susac syndrome, the pattern of GCIPL and RNFL losses may help differentiate it from MS (16–19).
3. Differentiation of subtypes of MS: Various researches have shown more RNFL thickness reduction as well as macular volume decrease in ancillary continuous MS disease in comparison with the relapsing-remitting MS (RRMS) (20, 21).
4. Severity of MS disease: Microcystic macular edema in MS is associated with disease severity (22).
5. Clinical observation of MS disease: The course of the disorder is in sync with OCT parameters. Retinal changes in MS patients reflect pathology in the global central nervous system (23–25).
6. Biomarker: Depletion in GCIPL is in relation with intrathecal B-cell immunity and it represents an unconventional risk factor for exacerbating disability. In contrast, high inner nuclear layer (INL) volumes are associated with activity on magnetic resonance imaging in the brain parenchyma (26).
7. Evaluation of response to treatment: Rates of GCIPL atrophy with RRMS differs from one patient to another with respect to the use of disease-modifying therapy. OCT is used to monitor the brain damaging effects in the retina during treatment as a measure used in RRMS clinical trials (27).

OCT for evaluating physical disability in patients with Multiple Sclerosis

In recent years, studies demonstrated that modifications of OCT parameters are useful markers for assessing MS progression as well as its connection with increased physical disability (28–33). To analyze the relationship between continually increasing disability and RNFL deterioration, Garcia-Martin et al. (28) quantified RNFL modifications with 100 MS patients and 50 healthy subjects used as experimental control subjects, placed under a 5-year examination. OCT revealed changes in all RNFL thicknesses in both groups. Greater differences in the inferior and temporal RNFL thickness were found in both groups. In MS patients only, OCT showed that increase in the Expanded Disability Status Scale (EDSS) is moderately related to temporal and superior RNFL thinning. Temporal RNFL thinning based on OCT results was moderately connected with degraded quality of life (QOL). The authors showed that RNFL thinning based on OCT results proves to be a useful marker for determining MS development and is related to increased disability and reduced QOL.

Toledo et al. (29), compared OCT and Heidelberg retinal tomography (HRT) techniques in relation with the measurement of the thickness of the RNFL in patients with MS and to investigate whether changes in the thickness of the RNFL is related to physical and mental disability. The

authors discovered that both OCT and HRT could clarify a depletion in the thickness of the RNFL in patients with MS in comparison with the control subjects. It was discovered that the degree of RNFL atrophy has a relationship with cognitive disability, especially with the symbol digit modality test. However, temporal quadrant RNFL atrophy determined using OCT was theoretically attributed to physical disability. El-Ayoubi et al. (30) demonstrated that, for early RRMS patients who did not undergo optic neuropathy, the level of retinal thickness was connected to physical disability and cognitive disability, supporting their potential as biomarkers of axonal loss. Abalo-Lojo et al. (31), explored the relationship between RNFL thickness and brain atrophy using magnetic resonance imaging (MRI) with bicaudate ratio (BCR). Their study included 59 controls and 88 MS patients with different level of disease severity (11 with clinically isolated syndrome (CIS), 68 with RRMS, and 9 with secondary progressive MS). They also determined whether RNFL thickness is related to EDSS score. Patients with MS (0.12 ± 0.03) displayed a higher BCR than control subjects (0.08 ± 0.009). OCT average RNFL thickness in patients with MS was significantly lower ($84.51 \pm 14.27 \mu\text{m}$) than in control subjects ($98.44 \pm 6.83 \mu\text{m}$). For patients with MS without optic neuritis, there was a correlation between BCR and OCT average RNFL thickness. There was a significant relationship between average RNFL thickness and the EDSS score. This study showed that RNFL thickness correlates with BCR and with MS subtypes. In addition, retinal axons damage is apparently related to brain damage in patients with MS. The role of the peripapillary retinal nerve fiber layer (pRNFL) thickness and the macular volume in eyes without prior history of optic neuritis were assessed in a multicenter, cohort study, as the biomarkers of exacerbating disability in patients with multiple sclerosis with one or both eyes having no optic neuritis. Included in the primary analyses were 879 patients with clinically isolated syndrome ($n=74$), RRMS ($n=664$), or progressive MS ($n=141$). Disability exacerbation was found in 252 (29%) of 879 patients with MS relative to a subsequent follow-up for 2.0 years (range 0.5–5 years). Patients with a pRNFL of less than or equal to $87 \mu\text{m}$ or less than or equal to $88 \mu\text{m}$ presented twice the risk of increasingly declining disability within the second and third year of follow-up (hazard ratio 2.06, 95% CI 1.36–3.11; $p=0.001$). The risk escalation was up to four times the previous state after the third year and up to the end of the fifth year of follow-up (3.81, 1.63–8.91). The authors failed to determine any significant correlation for macular volume. Their research outcomes provided affirmation that monitoring pRNFL thickness by OCT is useful for estimating the danger of intensifying disability over time in MS patients (32).

Sanchez-Dalmau et al. (33) carried out a cross-sectional successive examination of 119 patients with MS (65 with ON, 54 without ON). The authors assessed the patients' perception of the quality of their vision using color vision, high contrast visual acuity, and 2.5% and 1.25% low contrast visual acuity. Standard of vision was reported by the patient based on the uniqueness of individual visual impression and was assessed with the Visual Functioning Questionnaire-25 (VFQ-25) with 10 neuro-ophthalmologic items. MS disability was determined using the EDSS, the MS functional composite (MSFC), and the brief repetitive battery-neuropsychology (BRB-N). Retinal atrophy (pRNFL and GCIPL) were in close relation with impaired low contrast vision as well as color vision, and the level of the GCIPL is apparently related to visual quality. Multiple regression analysis showed that the EDSS score was an illustrative parameter for high contrast vision sequel to subsequent analyses; GCIPL volume was explanatory for low quality vision, as well as GCIPL level and EDSS were illustrative for color vision. The illustrative parameters of visual quality were high contrast vision and color vision. The authors concluded that visual quality in MS patients is relative to the disability in high contrast visual clarity and color vision as a result of the disorder.

Limitations of OCT

In spite of the fact that OCT is broadly utilized in routine clinical practice,

it has a few restrictions. It has a little measure of normative data for which the quantity of samples is constrained (256 eyes of 123 patients). The mean age of the samples is 51.51 (territory: 20–87 years). Gaps in Bruch's membrane deposits were manually affirmed. Also, only the posterior segment of the retina and the optic disc can be clearly assessed. Picture quality is influenced by corneal edema and lens and vitreous opacity (1–3).

Optical coherence tomography angiography and MS

OCT angiography (OCT-A) is a comparatively new, non-invasive outpatient visual representation test that provides both structural and functional information about the macula. OCT-A is used for patients who present retinal vascular disorder, choroidal vascular disorder, and ophthalmic oncology. Its importance is apparently realized in patients with other macular and retinal diseases as well as optic nerve diseases and glaucoma (34–36). Wang et al. (37), demonstrated that OCT-A could be useful in investigation retinal pathology in MS patients. Lanzillo et al. (38), evaluated assessed the presence of retinal vascular irregularities in 50 MS patients who underwent ON and those who have no history of ON along side 46 healthy subjects. The authors examined the relationship between clinical history, EDSS, Multiple Sclerosis Severity Score (MSSS), and disease duration and, OCT-A. OCT-A demonstrated a decline in vessel thickness in the eyes of MS patients in comparison with that of the controls. A statistically important decrease in all SD-OCT and OCT-A parameters were observed in the eyes of patients who underwent ON and those who have no history of ON when compared with control eyes. They reported a negative relationship between SD-OCT parameters and MSSS as well as between vessel density parameters and EDSS. They suggested that OCT-A is most likely a good marker of disorder as well as impairment in MS.

CONCLUSION

OCT is a relatively cheaper, non-invasive imaging system. OCT is approved in MS, and research have shown its clinical importance at both the individual level and a more extensive research level. OCT has the extraordinary capacity to quantify axons and might be important for use in clinical trials of neuroprotective treatments. It can possibly enhance the various ways of perception, diagnosis, monitoring, and treating MS.

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