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Review article

Optical coherence tomography in diagnosis and monitoring multiple sclerosis

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ABSTRACT

This paper presents application of optical coherence tomography (OCT) for diagnosis and monitoring of multiple sclerosis (MS). The peripapillary retinal nerve fibre layer thinning and the reduced total macular volume analysis are shown. With the course of the MS, the severity of these abnormalities increases which reflects the progressive degeneration of retinal ganglion cells and nerve fibres. The OCT parameters are sensitive, non-invasive indicators useful in assessing the progression of inflammation and neurodegeneration in MS.

1. Introduction

Multiple sclerosis (MS) is an inflammatory and neurodegenerative disorder of the central nervous system (CNS). The disease involves the presence of demyelinating lesions and axonal loss associated with the demise of oligodendrocytes and astrogliotic proliferation, as well as neurodegeneration. As a result, multifocal CNS damage occurs disseminated in space and time, leading to severe neurological deficits and disability. Although both inflammation and nerodegeneration play a role in MS, the dynamics of the two processes differs. In the early stages of the disease the inflammatory processes predominate. With disease progression, they slow down whereas the axonal degeneration, which is the main cause of MS-related disability,

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accelerates [1–3]. Neurological symptoms of MS are not pathognomonic for the final diagnosis. The main diagnostics criteria include the confirmed multifocal lesions and the onset of individual symptoms at different points in time and space [4]. The presentation of cerebrospinal fluid oligoclonal bands, abnormal evoked potential and multifocal lesions in magnetic resonance imaging (MRI) enabled faster diagnosis [4,5].

The interdependence between focal inflammation, diffuse inflammation, and neurodegeneration as well as their relative contribution to clinical deficits remains ambiguous [6]. As the damage of oligodendrocytes would lead to the pathology of MS, its elimination is favourable for preventing axonal degeneration [7,8].

Optical coherence tomography (OCT) is a non-invasive tool used in MS as a potential marker of axonal retinal degeneration. Retinal nerve fibre layer (RNFL) thickness and total macular volume (TMV) are the most frequently investigated OCT parameters.

2. Retina and the optic nerve

The retina is a unique structure in a human visual system. It is developmentally related to the cerebrum, as it differentiates from the two layers of the optic cup, which is the prominence of the neural tube. Hence, considering the retina is a part of the CNS, it can be divided into two integral parts: the first, neuroepidermal one, which includes rods and cones forming the first neuron; and the second, cerebral one, which includes bipolar and ganglion cells forming the second and third neuron of the optic tract. The axial extensions of ganglion cells form the nerve fibre layer, stretching to the optic disc, where they leave the eye as an optic nerve consisting of 1.0–1.2 million of non-myelinated axons of retinal ganglion cells. It enters the orbit through the scleral lamina cribrosa, where the myelin sheaths of the nerve fibres originate. Histologically, the optic nerve, which contains axons of ganglion cells, astrocytes, oligodendrocytes and microglia, shows higher resemblance of the white matter of the brain rather than of the peripheral nerve [9]. The RNFL contains only the axons of ganglion cells and glia, without the myelin sheath, which contributes to its uniqueness. Hence, the RNFL thickness measurement detects the actual axonal injury and the results remain unaffected by the presence and thickness of the myelin sheath. That is way the RNFL may be the location of choice for the monitoring and assessment of neurodegeneration.

Axonal and neuronal damage are widely accepted as key events in the disease course of MS. In clinical practice, patients presenting with first clinical event that is highly indicative of MS are often diagnosed with clinically isolated syndrome (CIS). Oberwahrenbrock et al. shows that retinal neurodegeneration is already detectable in CIS patients and is dependent but importantly also independent of clinical relapses i.e. optic neuritis (ON). The present study is the first to investigate intraretinal layer changes or detect retinal neurodegeneration independent from ON in a larger cohort of CIS patients. Azevedo et al. indicates that the thalamus may be a location of early neurodegeneration in MS. Their data identified the presence of thalamic atrophy in radiologically isolated syndrome (RIS), which is highly indicative of early CNS demyelinating disease and should be investigated as a metric associated with neurodegeneration [10].

The post-mortem analyses report retinal pathology in MS beyond damage to the RNFL and the ganglion cell layer (GCL). They indicate that retinal pathology might not only develop as a consequence of inflammatory attack to the anterior optic pathway causing retrograde axonal and neuronal degeneration with RNFL thinning and retinal GCL, but retina itself may be a primary target of degenerative or inflammatory processes. Thus, OCT is increasingly being utilised as a marker of axonal loss in MS treatments trials [11].

3. Optical coherence tomography: biophysical basis of diagnostic imaging

The OCT is the method, which enables the imaging of axonal loss and injury to the retinal ganglion cells. It is a modern technique for tissue cross-sectional imaging first described in 1991 by Huang et al. from the Fujimoto Laboratory at the Massachusetts Institute of Technology, USA [12]. The subsequent development was rapid and spectacular – the first in vivo human cross-sectional retinal measurements were taken in 1993 at the University of Vienna, and in 1996, the Carl Zeiss Meditec company presented the first commercially available time-domain OCT (TdOCT). Then, the Institute of Physics at the Nicolaus Copernicus University, Poland entered the stage. Here, the first spectral domain optical coherence tomography (SOCT) for the in vivo retinal imaging was developed in 1999. In 2002, the first in vivo tomograms of the human eye were obtained by the same researchers [13,14]. OCT is basically similar to the ultrasonography examination. The difference, however, lies in using the light waves (instead of the sound wave) for tissue penetration. Like in ultrasound, the wave return time is measured, after it has been reflected and scattered throughout the imaged tissue. As the scanning beam velocity is very high (the light wave velocity is approx. 300,000 km/s, as compared to the velocity of the sound in water of 1500 m/s), a direct measurement of the wave return time is virtually impossible. Instead, wave interference is utilised for these measurements. OCT can be classified according to the measurement method into the originally developed TdOCT, and a newer SOCT. In TdOCT, the reference mirror is movable. By changing its distance from the photodetector it is possible to compare the light beam reflected by the mirror to the light beam returning from the eye. It enables a precise assessment of distances and a thickness of individual tissue structures. In SOCT, a movable reference mirror is absent and the diffractive grid is introduced and a light beam measurement is taken differently, utilising the Fourier transform [15]. As a result, the SOCT images yield much higher resolution, and the acquisition time of a single 1024-point line (a single A-scan) is only 19 microseconds, being 250-fold shorter as compared to TdOCT.

4. TdOCT ver. SOCT in retinal evaluation

TdOCT is a method, which enables acquisition of lower resolution retinal tomograms, as compared to the SOCT, with

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