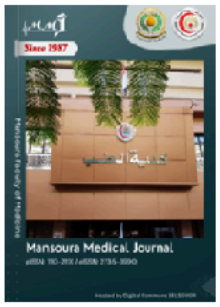
MANSOURA MEDICAL JOURNAL

ISSN - Print: 1110-211X - Online: 2735-3990

journal homepage: mmj.mans.edu.eg



Volume 53 | Issue 1 Article 11

Value of Optical Coherence Tomography and Optical Coherence Tomography Angiography in Relation to Disability Progression in Multiple Sclerosis Patients

Hossam Abd El-Nasser Kamal

Resident of neurology, Ministry of Health, Egypt., hossam9nasser@gmail.com

Ahmed Effat Abbas Mohamed Saeid

Lecturer of neurology, Mansoura faculty of Medicine.

Amgad Mahmoud El Nokrashy

Lecturer of ophthalmology, Mansoura faculty of Medicine.

Mohamed Galal El-Khateeb

Professor of neurology, Mansoura faculty of Medicine

ORIGINAL STUDY

Value of Optical Coherence Tomography and Optical Coherence Tomography Angiography in Relation to Disability Progression in Multiple Sclerosis Patients

Hossam Abdel Nasser [a,*], Ahmed Saied [a], Amgad El Nokrashy [b], Mohammed G. El-Khateeb [a]

[a] Department of Neurology, Faculty of Medicine, Mansoura University, Egypt
[b] Department of Ophthalmology, Faculty of Medicine, Mansoura University, Egypt

Abstract

Background: **Optical coherence tomography (OCT) and OCT-angiography (OCT-A) permit quantification of retinal layer atrophy relevant to multiple sclerosis (MS) progression.**

Methods: **We conducted this case−control study to assess of the changes in OCT and OCTA measures in relation to the duration of MS and the expanded disability status scale (EDSS). A total of 70 MS patients compared with 35 healthy controls were enrolled.**

Results: **According to OCT findings, there was a significantly lower mean value of retinal nerve fiber layer thickness (RNFL) and ganglion cell complex (GCC) in the MS patients group compared with the control group with *P* less than 0.001. Cases with an EDSS greater than 1.5 exhibited significantly lower average values of RNFL and GCC. The mean RNFL values were 82.29 ± 17.21 compared with 98.31 ± 9.17, and the mean GCC values were 82.57 ± 4.95 in contrast to 95.02 ± 7.25. The patients' group had a significantly lower mean value of all OCT-A measurements than the control group ($P < 0.05$) except for fovea. Cases with an EDSS greater than 1.5 had a statistically significant lower mean value of whole image, parafovea, superior and inferior hemispheres compared with cases with no disability EDSS less than or equal to 1.5.**

Conclusion: **We found that MS patients' retinas had thinner retinal layers and less dense blood vessels. We highlighted the important clinical relationship that exists between vascular density, EDSS, and retinal layer thickness. This suggests that OCT and angio-OCT may be useful markers of MS patients' impairment and disease progression.**

Keywords: Expanded disability status scale, Multiple sclerosis, Optical coherence tomography, Optical coherence tomography angiography

1. Background

Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease of the central nervous system (CNS), resulting in lifelong neurological disability. MS affects the retina and the visual pathway. Chronic inflammation combined with acute demyelinating optic neuritis (ON), or optic nerve demyelination, can have both direct and indirect effects on the visual pathway (Toosy et al., 2014).

As part of the nervous system, the retinae of people with MS show inflammatory and neurodegenerative alterations. There is growing evidence that retinal abnormalities, particularly neurodegeneration, parallel global CNS alterations in MS (Brandt et al., 2017).

Abbreviations: DCP, Deep capillary plexus; EDSS, Expanded disability status scale; GCC, Ganglion cell complex; MS, Multiple sclerosis; OCT, Optical coherence tomography; OCT-A, OCT-angiography; RNFL, Retinal nerve fiber layer thickness; RRMS, Relapsing remitting MS; SCP, Superficial capillary plexus; SVP, the superficial vascular plexus; VD, Vessel density.

Received 28 November 2023; revised 18 December 2023; accepted 20 December 2023.
Available online 6 May 2024

* Corresponding author at: Department of Neurology, Faculty of Medicine, Mansoura University, 35516, Egypt. Fax: +0503688146.
E-mail address: hossam9nasser@gmail.com (H.A. Nasser).

https://doi.org/10.58775/2735-3990.1406

Using near-infrared light, optical coherence tomography (OCT) is a noninvasive medical technology that creates two- or three-dimensional pictures of tissues, including the retina (Hrynchak and Simpson, 2000). It is affordable, quick, well-tolerated, and reproducible. Numerous researches have looked into how OCT measures can help us better understand the pathobiology of MS and find new biomarkers to track the disease's neurodegeneration and response to treatment (Brandt et al., 2017).

A new advance in OCT technology is retinal optical coherence tomography angiography (OCT-A), which offers a fast, and affordable way to examine the retinal vascular system. The ability to scan vascular anatomy and, subsequently, the metabolic requirement of the retina may open up new avenues for MS research. Alterations in this structure may be crucial for anterior pathway suffering, which can range from inflammation to neurodegeneration (Wang et al., 2018; Kashani et al., 2021). According to OCTA investigations in MS, there is a decrease in the densities of the retinal vasculature, principally in the superficial vascular plexus (SVP) (Pujari et al., 2021).

The expanded disability status scale (EDSS) is one of the most often used methods for evaluating the stages and course of illness. The EDSS enables medical professionals to evaluate the states of patients' illnesses. A higher score denotes greater damage to the condition (Kurtzke, 2015).

In patients with MS, relationships between OCT, OCTA measurements, and disability (EDSS) score have been proposed. As a biomarker of functional impairment in MS, retinal layer thicknesses and SVP density may provide relevant information (Britze and Frederiksen, 2018).

2. Methods

This was a case–control study, conducted at the Ophthalmology and Neurology Departments, MS outpatients, Mansoura University Hospital from October 2021 until April 2023. We included 35 healthy controls and 70 MS patients diagnosed depending on the 2017 revised McDonald Criteria (Thompson et al., 2018).

2.1. Inclusion and exclusion criteria

The study concerned patients who were diagnosed with MS fulfilling the criteria of the 2017 revised McDonald Criteria and aged 18 years old and more. The following patients were not included in our analysis: a) those with a history of retinal detachment or retinal vascular occlusion, glaucoma, or other known other neurological or ophthalmological diseases, b) those who had previously undergone ocular surgery or eye trauma, c) those with high refractive errors, and d) uncontrolled hypertension or diabetes mellitus.

2.2. Sampling method

A convenient sample of 35 healthy controls (matched for age and sex) and 70 MS patients were enrolled in our study. The patients were then split into two groups based on the EDSS: those without disabilities (EDSS $\leq$1.5) and those with disabilities (EDSS >1.5).

2.3. History and examination

(1) A detailed history according to MS unit sheet Mansoura University Hospital with special emphasis on onset of disease, presenting symptoms, and disease progression.
(2) Neurological examination: complete neurological examination with emphasis on common neurological disorders related to MS disease.
(3) Ophthalmological examination.

2.4. Measuring disability progression of disease using EDSS score

The EDSS scale is the most often utilized in MS patients. The EDSS is a fairly effective means of assessing impairment. The EDSS assigns a total score from 0 to 10 on a 10-point scale. A normal neurological examination yields a score of 0, while MS-related deaths get a score of 10 (Kurtzke, 2015)

2.5. OCT of retinal layers thicknesses

Real-time cross-sectional retinal imaging is provided by OCT, a noninvasive tool. OCT creates a cross-sectional map of the retina that is accurate to within 10–15 microns by using the concept of interferometry.

2.6. OCTA of retinal vasculature 'ocular imaging using swept Source-OCTA'

Topcon DRI-OCT Triton Swept Source OCT (Japan) Swept-source-OCTA (SS-OCTA) macular volume scans of 3 $\times$ 3 mm were used to image every patient in the study. Retinal thicknesses, both total and differential, were measured. With a semi-automated method, the vessel density (VD) was determined.

2.7. Statistical analysis

The statistical software for social sciences, version 26.0 (SPSS Inc., Chicago, Illinois, USA), was used to evaluate the recorded data. The ranges and mean ± standard deviation (SD) of the quantitative data were displayed. We compared the mean values using the student *t*-test (t). To further compare the preintervention and postintervention groups, the paired *t*-test was utilized. In order to ascertain relationships between variables, correlation analysis was performed using the Pearson correlation coefficient (r). In this investigation, the significance level was determined to be 0.05 ($P < 0.05$).

3. Results

The study comprised of 70 MS patients and 35 healthy controls. The mean age of the MS patients was 32.94 ± 9.89, while the control group's mean age was 35.29 ± 10.45. Of the patients that were included, 21 females were in the control group and 50 females were in the MS group.

In comparison with the control group, the MS patients' group had significantly lower mean values of RNFL and GCC, with a *P* value of less than 0.001, as showed by Table 1.

Table 2 demonstrates that the patient group had a statistically significant higher mean value of vessel density of fovea (*P* value < 0.001) than the control group, but the patient group had a statistically significant lower mean value of OCT-A vessel densities about all other retinal sectors than to the control group.

With a *P* value less than 0.001, Table 3 demonstrates a very statistically significant lower mean value of RNFL and GCC in the EDSS greater than 1.5 group as compared with the EDSS less than or equal to 1.5 group.

In comparison with the EDSS less than or equal to 1.5 group, Table 4 demonstrates a statistically significant decreased mean value of the vessel density

Table 1. Comparison between multiple sclerosis patients and control group according to Optical coherence tomography investigations.

Investigations OCT	MS patients Group ($n = 70$)	Control group ($n = 35$)	Test value	*P*-value
RNFL	91.90 ± 15.11	102.63 ± 6.41	16.122	<0.001**
GCC	90.04 ± 8.87	100.54 ± 5.45	41.185	<0.001**

Using: t-Independent Sample t-test for Mean ±SD; p-value >0.05 is insignificant; **P*-value <0.05 is significant; ***P*-value <0.001 is highly significant,RNFL: Retinal nerve fiber layer thickness,GCC: Ganglion cell complex.

Table 2. Comparison between the multiple sclerosis patients and control group according to vessel density (VD) assessed by Optical coherence tomography angiography.

Optical coherence tomography angiography	Multiple sclerosis patients ($n = 70$)	Control group ($n = 35$)	Test value	*P*-value
Whole image	275.63 ± 40.74	291.40 ± 9.23	4.238	0.031[a]
Fovea	266.86 ± 36.75	241.63 ± 25.34	6.302	<0.001[b]
Parafovea	299.17 ± 17.47	316.31 ± 12.82	26.501	<0.001[b]
Superior hemisphere	303.51 ± 16.77	316.29 ± 13.16	15.505	<0.001[b]
Inferior hemisphere	304.91 ± 18.46	316.97 ± 17.25	10.390	0.002[a]
Temporal	298.81 ± 16.96	306.51 ± 17.72	4.670	0.033[a]
Superior	285.30 ± 28.31	314.09 ± 17.28	30.428	<0.001[b]
Nasal	275.23 ± 42.19	316.94 ± 17.65	31.341	<0.001[b]
Inferior	301.89 ± 17.71	315.09 ± 17.86	12.890	<0.001[b]

P value greater than 0.05 is insignificant.
[a] *P* value less than 0.05 is significant.
[b] *P* value less than 0.001 is highly significant.

Table 3. Comparison between no disability group Expanded disability status scale less than or equal to 1.5 and disability group Expanded disability status scale greater than 1.5 according to Optical coherence tomography investigations.

Investigations Optical coherence tomography	EDSS ≤1.5 group ($n = 42$)	EDSS >1.5 group ($n = 28$)	Test value	*P*-value
RNFL	98.31 ± 9.17	82.29 ± 17.21	5.062	<0.001**
GCC	95.02 ± 7.25	82.57 ± 4.95	7.926	<0.001**

P-value >0. 05 is insignificant; **P*-value <0. 05 is significant; ***P*-value <0. 001 is highly significant, EDSS: Expanded disability status scale, RNFL: Retinal nerve fiber layer thickness,GCC: Ganglion cell complex.

Table 4. Comparison between no disability group Expanded disability status scale less than or equal to 1.5 and disability group Expanded disability status scale greater than 1.5 according to vessel density (VD) assessed by Optical coherence tomography angiography.

Optical coherence tomography angiography	EDSS ≤1.5 group (n = 42)	EDSS >1.5 group (n = 28)	Test value	P-value
Whole image	288.07 ± 22.68	256.96 ± 53.46	3.354	<0.001[b]
Fovea	273.24 ± 38.28	257.29 ± 32.66	1.808	0.075
Parafovea	305.74 ± 15.81	289.32 ± 15.26	4.315	<0.001[b]
Superior hemisphere	311.60 ± 14.20	291.39 ± 12.58	6.097	<0.001[b]
Inferior hemisphere	310.17 ± 15.03	297.04 ± 20.50	3.091	0.003[a]
Temporal	306.50 ± 15.51	287.29 ± 11.83	5.561	<0.001[b]
Superior	292.93 ± 25.57	273.86 ± 28.79	2.907	0.005[a]
Nasal	280.07 ± 39.53	267.96 ± 45.67	1.179	0.242
Inferior	308.12 ± 16.38	292.54 ± 15.59	3.974	<0.001[b]

P value greater than 0.05 is insignificant.
[a] P value less than 0.05 is significant.
[b] P value less than 0.001 is highly significant.

of whole image, parafovea, superior hemisphere, inferior hemisphere, temporal, superior, and inferior with a P value less than 0.05.

With P value P less than 0.001, there was a statistically significant negative association found between EDSS and OCT research about RNFL and GCC. Additionally, Table 5 shows a statistically significant negative association (P value < 0.05) between EDSS and OCT angiography regarding the whole image, fovea, parafovea, superior and inferior hemispheres, and temporal aspects.

4. Discussion

The OCT results revealed that the MS patients' group had significantly lower mean values of RNFL and GCC than the control group. Also, our results revealed that cases with disability EDSS greater than 1.5 had a statistically significant lower mean value of RNFL 82.29 ± 17.21 versus 98.31 ± 9.17 compared with cases with no disability EDSS less than or equal to 1.5 cases. Also, OCT findings revealed that cases with disability (EDSS >1.5) had statistically significant lower mean value ganglion cell complex (GCC) 82.57 ± 4.95 versus 95.02 ± 7.25 compared with cases with no disability (EDSS≤1.5). Also, we reported a significant negative correlation between EDSS with OCT investigations about RNFL.

Table 5. Correlation between Expanded disability status scale with Optical coherence tomography investigations and Optical coherence tomography angiography (VD), using Spearman's rank correlation coefficient (rs).

Optical coherence tomography	Expanded disability status scale	
	r-value	P-value
OCT Investigations		
RNFL	−0.651	<0.001[b]
GCC	−0.845	<0.001[b]
OCT angiography		
Whole image	−0.427	<0.001[b]
Fovea	−0.252	0.036[a]
Parafovea	−0.507	<0.001[b]
Superior hemisphere	−0.642	<0.001[b]
Inferior hemisphere	−0.470	<0.001[b]
Temporal	−0.599	<0.001[b]
Superior	−0.409	<0.001[b]
Nasal	−0.185	0.124
Inferior	−0.547	<0.001[b]

Using: Spearman's rank correlation coefficient (rs) P value greater than 0.05 NS.
GCC, Ganglion cell complex; RNFL, Retinal nerve fiber layer thickness.
[a] P value less than 0.05 S.
[b] P value less than 0.001 HS.

A prior investigation conducted by Lambe and colleagues assessed the potential correlation between a baseline retinal OCT evaluation and the worsening of long-term impairment in MS patients. They came to the conclusion that a reduction in baseline GCC thickness on OCT is independently linked to a deterioration of long-term impairment in MS patients (Lambe et al., 2021). In line with our research, Rothman and colleagues found that among MS patients in the lowest baseline total macular volume—of which the GCC is a significant portion—there was a roughly 3.5-fold higher chance of EDSS worsening during a 10-year period (Rothman et al., 2019). Martinez-Lapiscina and colleagues using SD-OCT, observed an increased risk of MS disability evolution over three to five years of follow-up using a cutoff of 87–88 pm (depending on the OCT device used) for baseline RNFL thickness (Martinez-Lapiscina et al., 2016). Similarly, another study by Balkç and colleague compared retinal alterations and microvascular abnormalities. They stated that there were notable variations between the MS subjects and the control group in the RNFL and GCC (Balõk et al., 2021). This validates the results of additional research conducted by Lanzillo and colleagues who proved that all GCC and RNFL

measures were shown to be lower in the patients compared with the controls group. Additionally, there was a negative relationship between the EDSS and OCT parameters (Lanzillo et al., 2018). This study agreed with our study in terms of the negative correlation between OCT parameters and EDSS. A study conducted by Oberwahrenbrock and colleagues. They discovered that, regardless of the MS subtype for all subtypes, the eyes of MS patients significantly reduced both RNFL thickness and total macular volume in comparison with controls (Oberwahrenbrock et al., 2012).

We showed that in MS patients, lower retinal vascular densities as observed by OCT-A were linked to a greater EDSS score and a higher probability of a clinically significant worsening of the EDSS. Furthermore, the results of OCT angiography revealed that the MS patients had a statistically significant lower mean value for OCT angiography in the whole image, parafovea, superior hemisphere, inferior hemisphere, temporal, superior, nasal, and inferior when compared with the control group.

Also, OCT angiography findings revealed that cases with disability (EDSS >1.5) had a statistically significant lower mean value of the whole image, parafovea, superior hemisphere, inferior hemisphere, temporal, and inferior compared with cases with no disability (EDSS $\leq$1.5) with *P*-value less than 0.05. A significantly negative correlation was observed between OCT-A and EDSS about Whole image, Fovea, Parafovea, Superior hemisphere, Inferior hemisphere, Temporal Superior and Inferior.

To the best of our knowledge, several studies tried to explain alterations that coexist in retinal microvasculature and retinal layers in MS and correlated with disease evolution. Our findings are consistent with the conclusions of Mohammadi and colleagues. They found that the retinas in MS patients are more likely to show decreased vascular density in the macular and optic disc areas, mainly in superficial capillary plexus, that was validated by measurements of MS patients (Mohammadi et al., 2023). Khader and colleagues evaluated the results of OCTA in MS. They concluded that the OCT-detected damage to the RNFL and GCC is substantially connected with decreased vascularity of the optic nerve in MS (Khader et al., 2021). Cordon and colleagues. Examined the superficial retinal microvascular plexuses in MS patients that were identified by OCT-A and contrasted them with controls. According to their findings, it is not necessary for optic nerve inflammation to be present for changes in retinal vascularization to be seen in MS patients (Cordon et al., 2020). Murphy and colleagues investigated associations between visual function and overall impairment and compared the retinal vessel densities in MS patients and controls. They came to the conclusion that there is a reduction in the density of retinal SVP, as determined by OCTA, in MS eyes. This reduction is correlated with visual function and EDSS (Murphy et al., 2020).

Abnormality detected in cerebral and retinal vascular measurements in multiple sclerosis may, in fact, be a reflection of neurodegeneration. The mechanism behind decreases in retinal vasculature density in MS is one of the main questions raised by this study and others. Therefore, a number of research attempted to explain these changes in the retinal layers and microvasculature in MS and how they relate to the course of the disease Diffuse retinal microvascular loss was also observed by Jiang and colleagues in MS patients. This loss could be a signpost for the loss of RNFL and GCC, and it could be explained in part by the reduced metabolic demand caused by the loss of retinal neurons (Jiang et al., 2020).

4.1. Conclusion

We have shown that lower OCT-identified RNFL and GCL thicknesses, as well as lower OCTA-identified retinal vascular densities, corresponded with greater EDSS and predicted a clinically meaningful decline in EDSS. Our results contribute to the increasing amount of data indicating OCT-derived retinal measurements and OCT-A are effective indicators of global neurodegeneration in MS patients. With the approaching era of possibly neuroprotective and neurorestorative therapy for MS patients, measurement of these cheap, easily obtained biomarkers will be crucial in clinical and research contexts.

Publication ethical statement

All patients gave their informed consent for inclusion before they participated in this study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by IRB (MS. 21.05.1515. R1. R2. R3-2021/07/01).

Conflicts of interest

There are no conflicts of interest.

Acknowledgments

We acknowledge every person helped us with finishing this study. We want also to thank the

department of ophthalmology; without them we could not be able to do the investigation of the study. We can't forget the precious help of nurses in outpatient clinic of neurology in Mansoura University Hospitals.

References

Balõkcõ, A., Parmak Yener, N., Seferoğlu, M., 2021. Optical coherence tomography and optical coherence tomography angiography findings in multiple sclerosis patients. Neuro Ophthalmol. 46, 19–33.

Brandt, A.U., Martinez-Lapiscina, E.H., Nolan, R., Saidha, S., 2017. Monitoring the course of MS with optical coherence tomography. Curr. Treat. Options Neurol. 19 (4), 15.

Britze, J., Frederiksen, J.L., 2018. Optical coherence tomography in multiple sclerosis. Eye (Lond) 32, 884–888.

Cordon, B., Vilades, E., Orduna, E., Satue, M., Perez-Velilla, J., Sebastian, B., et al., 2020. Angiography with optical coherence tomography as a biomarker in multiple sclerosis. PLoS One 15, e0243236-e0243236.

Hrynchak, P., Simpson, T., 2000. Optical coherence tomography: an introduction to the technique and its use. Optom. Vis. Sci. 77, 347–356.

Jiang, H., Gameiro, G.R., Liu, Y., Lin, Y., Hernandez, J., Deng, Y., et al., 2020. Visual function and disability are associated with increased retinal volumetric vessel density in patients with multiple sclerosis. Am. J. Ophthalmol. 213, 34–45.

Kashani, A.H., Asanad, S., Chan, J.W., Singer, M.B., Zhang, J., Sharifi, M., et al., 2021. Past, present and future role of retinal imaging in neurodegenerative disease. Prog. Retin. Eye Res. 83, 100938.

Khader, S.A., Nawar, A.E., Ghali, A.A., Ghoneim, A.M., 2021. Evaluation of optical coherence tomography angiography findings in patients with multiple sclerosis. Indian J. Ophthalmol. 69, 1457–1463.

Kurtzke, J.F., 2015. On the origin of EDSS. Mult Scler Relat Disord 4, 95–103.

Lambe, J., Fitzgerald, K.C., Murphy, O.C., Filippatou, A.G., Sotirchos, E.S., Kalaitzidis, G., et al., 2021. Association of spectral-domain OCT with long-term disability worsening in multiple sclerosis. Neurology 96, e2058–e2069.

Lanzillo, R., Cennamo, G., Criscuolo, C., Carotenuto, A., Velotti, N., Sparnelli, F., et al., 2018. Optical coherence tomography angiography retinal vascular network assessment in multiple sclerosis. Mult. Scler. J 24, 1706–1714.

Martinez-Lapiscina, E.H., Arnow, S., Wilson, J.A., Saidha, S., Preiningerova, J.L., Oberwahrenbrock, T., et al., 2016. Retinal thickness measured with optical coherence tomography and risk of disability worsening in multiple sclerosis: a cohort study. Lancet Neurol. 15, 574–584.

Mohammadi, S., Gouravani, M., Salehi, M.A., Arevalo, J.F., Galetta, S.L., Harandi, H., et al., 2023. Optical coherence tomography angiography measurements in multiple sclerosis: a systematic review and meta-analysis. J. Neuroinflammation 20, 85–90.

Murphy, O.C., Kwakyi, O., Iftikhar, M., Zafar, S., Lambe, J., Pellegrini, N., et al., 2020. Alterations in the retinal vasculature occur in multiple sclerosis and exhibit novel correlations with disability and visual function measures. Mult. Scler. 26, 815–828.

Oberwahrenbrock, T., Schippling, S., Ringelstein, M., Kaufhold, F., Zimmermann, H., Keser, N., et al., 2012. Retinal damage in multiple sclerosis disease subtypes measured by high-resolution optical coherence tomography. Mult Scler Int 2012, 1–15.

Pujari, A., Bhaskaran, K., Sharma, P., Singh, P., Phuljhele, S., Saxena, R., et al., 2021. Optical coherence tomography angiography in neuro-ophthalmology: current clinical role and future perspectives. Surv. Ophthalmol. 66, 471–481.

Rothman, A., Murphy, O.C., Fitzgerald, K.C., Button, J., Gordon-Lipkin, E., Ratchford, J.N., et al., 2019. Retinal measurements predict 10-year disability in multiple sclerosis. Ann Clin Transl Neurol 6, 222–232.

Thompson, A.J., Banwell, B.L., Barkhof, F., Carroll, W.M., Coetzee, T., Comi, G., et al., 2018. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 17, 162–173.

Toosy, A.T., Mason, D.F., Miller, D.H., 2014. Optic neuritis. Lancet Neurol. 13, 83–99.

Wang, L., Murphy, O., Caldito, N.G., Calabresi, P.A., Saidha, S., 2018. Emerging applications of optical coherence tomography angiography (OCTA) in neurological research. Eye Vis (Lond) 5, 11.