



NICOLAUS COPERNICUS  
UNIVERSITY  
IN TORUŃ



**Quality in Sport. eISSN 2450-3118.**

**Journal Home Page**

**<https://apcz.umk.pl/QS/index>**

**KRÓL, Agata, MURASZEWSKA, Emilia, MURASZEWSKI, Łukasz, KWITOWSKA, Patrycja, UBYSZ, Eryk, LEWANDOWSKA, Edyta, LUCZYŃSKI, Cezary, PACZKOWSKI, Maciej, WRĘCZYCKI, Mariusz, and PYJECKA, Małgorzata. Optical Coherence Tomography (OCT) as a Retinal Biomarker for Brain Neurodegeneration: A Narrative Review. *Quality in Sport*. 2026;54:70115. eISSN 2450-3118. <https://doi.org/10.12775/QS.2026.54.70115>**

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).  
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.  
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2026.  
This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland. Open Access: This article is distributed under the terms of the Creative Commons Attribution Noncommercial License, which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits unrestricted, non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited.  
The authors declare that there is no conflict of interest regarding the publication of this paper.  
Received: 22.03.2026. Revised: 26.03.2026. Accepted: 30.03.2026. Published: 2.04.2026.

---

## **Optical Coherence Tomography (OCT) as a Retinal Biomarker for Brain Neurodegeneration: A Narrative Review**

**Agata Król**

Masovian Bródno Hospital

Kondratowicza 8, 03-242 Warsaw, Poland

<https://orcid.org/0009-0001-3461-4786>

akrol3088@gmail.com

**Emilia Muraszewska**

University Clinical Hospital in Poznań  
Przybyszewskiego 49, 60-355 Poznań, Poland  
<https://orcid.org/0009-0005-4534-1014>  
muraszewskaemilia@gmail.com

**Łukasz Muraszewski**

University Clinical Hospital in Poznań  
Przybyszewskiego 49, 60-355 Poznań, Poland  
<https://orcid.org/0009-0000-0331-9701>  
lukaszmuraszewski@outlook.com

**Patrycja Kwitowska**

Provincial Hospital in Poznań  
Juraszów 7/19, 60-479 Poznań, Poland  
<https://orcid.org/0009-0006-7297-2871>  
patrycjakwitowska@gmail.com

**Eryk Ubysz**

Provincial Polyclinical Hospital in Płock of Marcina Kacprzaka  
Medyczna 19, 09-400 Płock, Poland  
<https://orcid.org/0009-0004-9099-7648>  
eryk.ubysz123@gmail.com

**Edyta Lewandowska**

Central Clinical Hospital, University Clinical Center of the Medical University of Warsaw  
Banacha 1A, 02-097 Warsaw, Poland  
<https://orcid.org/0009-0006-1181-727X>  
e.a.b.lewandowska@gmail.com

**Cezary Łuczyński**

Multispecialist Provincial Hospital in Gorzów Wielkopolski

Jana Dekerta 1, 66-400 Gorzów Wielkopolski, Poland

<https://orcid.org/0009-0002-5128-4712>

czarek.1991@o2.pl

**Maciej Paczkowski**

Specialist Hospital Dr. Tytus Chałubiński

Lekarska 4, 26-610 Radom, Poland

<https://orcid.org/0009-0001-7670-1589>

mpaczkowskitbg@gmail.com

**Mariusz Wręczycki**

St Hedwig of Silesia Hospital in Trzebnica

Prusicka 53/55, 55-100 Trzebnica, Poland

<https://orcid.org/0009-0002-1945-4259>

mariuszwreczycki85@gmail.com

**Małgorzata Pyjecka**

Provincial Hospital of Ludwik Perzyna in Kalisz

Poznańska 79, 62-800 Kalisz, Poland

<https://orcid.org/0009-0002-5061-6359>

malgosia.pyjecka@gmail.com

Corresponding Author: Agata Król, akrol3088@gmail.com

**ABSTRACT**

**Background.** Optical coherence tomography is a rapidly developing imaging technique being increasingly used for the diagnosis of neurodegenerative diseases. It has brought forth new innovations for these diseases. Measurements of the retinal layers, macular and separate layer thicknesses, ganglion cell complex and choroidal thickness etc, have proven to be an excellent indication in differentiating these diseases using non-invasive and minimally invasive procedures.

**Aim.** To summarize available information and studies about the usage of OCT in neurodegenerative diseases which might create a new path for their diagnosis and treatment.

**Materials and Methods.** A literary search was done using the PubMed database to identify relevant studies published in English within the last 10 years. The selected studies were analysed to summarize current evidence regarding the potential role of OCT and OCTa in neurodegenerative diseases.

**Results.** Various studies have proven significant correlation between OCT measurements and neurodegenerative diseases. This increasingly developing correlation may help in the diagnosis and clinical treatment of these illnesses. However, there is a need for further studies and research to be conducted as non-specificity of OCT findings across the diseases remain a significant factor to be considered before mainstream usage.

**Conclusions.** OCT usage has proved to be a field which deserves more gravity towards it. The anatomical origin as well as similarity of the eye and brain in function may help us understand and diagnose these diseases better in the foreseeable future.

**Keywords:** RNFL thickness, Optical Coherence Tomography, Optical Coherence Tomography Angiography, Neurodegenerative disease, Alzheimer's Disease, Parkinson's Disease, Retina, CNS

## **1. Introduction**

Neurodegenerative diseases are illnesses that can affect both the central and peripheral nervous systems leading to impairment of cognition, motor, speech and even respiratory issues. These age-related issues are seen more in common recently.

Mild cognitive impairment (MCI), Alzheimer's disease (AD), Multiple sclerosis (MS), Parkinson's disease (PD) and Amyotrophic lateral sclerosis (ALS) have different pathophysiological mechanisms but have similar neuronal damage leading to partial or complete loss of functions [1].

Optical Coherence Tomography Angiography (OCT-A) is a newly introduced imaging technique used in a broad range of retinal vascular diseases mainly for the assessment of the integrity of the retinal vasculature. It has also been used for the assessment of blood perfusion of the optic nerve head in patients suffering from glaucoma [2].

The main pros of OCT are that patients don't have to be injected with a dye or have allergic reactions and suffer side effects i.e. anaphylaxis, nausea, vomiting, rash, urine and skin

discoloration. As a result, OCT is much safer and more comfortable for a patient when compared to fluorescein dye or indocyanine green angiography.

The brain and retinal vasculature structures hold striking resemblances of each other. The restrictions we face during examination of the vascular structure of the brain could possibly be solved by examining the changes that happen to the eye in neurodegenerative diseases. Blood flow in OCT imaging techniques is detected by repeated B scans of the same cross-sectional area using the flow of erythrocytes (RBCs).

MCI is seen as a possible middle ground between senescence and dementia which can show the mild issues of cognitive impairment without the interference of daily activities. Patients with amnesic MCI usually tend to develop higher rates of dementia later in their lives compared to other individuals who have no cognitive impairment [2].

Retinal microvascular changes including reduced vessel density in the superficial capillary plexus and deep capillary plexus along with decreased blood flow are some of the information we have from previously conducted studies noticed in patients with aMCI. Parafoveal and peripapillary densities were also significant findings in these studies which showed a positive correlation with low scores from Montreal Cognitive Assessment (MoCA). There is also a positive correlation between reductions in both vessel and perfusion densities of the superficial capillary plexus with measurements in brain volume seen in patients with MCI and AD.

## **2. Methods**

This paper is a narrative review. Research articles and studies conducted in the last 10 years were used from pubmed. Observational studies, narrative reviews, systematic reviews and meta-analyses were used in this paper. The search was done using a combination of keywords such as: “Optical Coherence Tomography”, “Optical Coherence Tomography Angiography”, “Neurodegenerative disease”, “Alzheimer's Disease”, “Parkinson's Disease”, “Multiple sclerosis”, “Progressive supranuclear palsy”, “Amyotrophic lateral sclerosis”, “Friedreich's ataxia”, “Adrenoleukodystrophy”, “Cerebral autosomal dominant arteriopathy with subcortical infarcts and Leukoencephalopathy”. The search and analysis of the available scientific literature were performed independently by each author. Studies from languages other than English were excluded.

### **3. Retina as an accessible component**

Shared embryology and anatomy is the basic link between retina and brain health. The retina can be considered an outgrowth of the diencephalon, making it an extension of the CNS. Additionally, it contains similar neuronal and vascular structures that are vulnerable to the same degenerative processes affecting the brain. These shared susceptibilities make the retina a perfect site for non-invasive monitoring of neurodegenerative changes [12].

### **4. Principles of OCT technology**

It is a type of optical biopsy. The main principle used here is the principle of low-coherence interferometry to measure reflected light and create high quality, quantitative images of the layers of retina.

OCT parameters and their importance:

- Retinal nerve fiber layer thickness (RNFL): They contain axons from retinal ganglion cells that form the optic nerve. Narrowing of the RNFL would mean axonal loss and is a recurring finding across many neurodegenerative diseases associated with cognitive deterioration and brain atrophy.
- Macular and separate layer thicknesses: Macular thickness is the distance between inner limiting membrane (ILM) and the retinal pigment epithelium (RPE) at the center of the retina. Apart from the RNFL, the OCT can measure more specific retinal layers which can offer a better insight to neurodegenerative illnesses.
- Ganglion cell complex: This refers to the ganglion cell layer (GCL) and inner plexiform layer (IPL). For example, in Alzheimer's disease the GCC inner plexiform complex is affected more compared to mild cognitive impairment.
- Inner retinal layer (IRL): It consists of RNFL, GCL, and IPL. The decline of dopaminergic amacrine cells may be the reason for IRL thinning in Parkinson's disease.
- The outer retinal layer (ORL): The ORL consists of the outer nuclear layer (ONL) and outer plexiform layer (OPL). They have shown diagnostic significance in distinguishing between Parkinsonian syndromes like progressive supranuclear palsy and multiple system atrophy [31].

OCTa develops a network of the retinal microvasculature, enabling us to measure vascular and perfusion metrics such as:

- Vessel density: In a given area the density of perfused blood vessels.

- Foveal Avascular zone: The central macular area which can be empty of capillaries and enlarged in illnesses like Alzheimer's [13,15].
- Radial Peripapillary Capillary (RPC) Density: The density of capillaries around the optic nerve head which may be reduced in dementia [14].
- Choroidal Thickness: A layer below the retina that is vascular. Thinning of the layer has been examined in Alzheimer's disease and may point towards the connected vascular pathology of the brain [16].

## **5. The reason for Retinal-CNS connection**

Shared degenerative mechanisms provide an insight to the connection between retinal changes and brain pathology. The neurodegenerative processes in the brain such as protein accumulation, neuroinflammation and loss of neurons are seen with changes in the retina due to its Central nervous system origin. For example, apoptosis of retinal ganglion cells leads to RNFL thinning, which can show the gray and white loss of volume in the visual pathways of the brain. Another non-invasive window to the CNS includes the microvascular differences in the retina such as reduced vessel density which may mirror cerebral small vessel disease [17,18].

## **6. Optical Coherence Tomography in Neurodegenerative Diseases**

### **6.1 Alzheimer's Disease**

Alzheimer's disease is the most commonly occurring subtype of dementia, and the most common causation of dependence and disability. According to estimates, one in three persons born in a first world country will develop dementia at some point in their life [27].

It is characterised as a progressive and irreversible dysfunction of cognitive abilities because of nerve cell apoptosis and brain atrophy. The most strongly associated factors of cognitive impairment being Cerebral neuronal loss and small-vessel cerebrovascular changes are hard to detect with the brain imaging modalities already available.

The CNS includes the retina which is connected to by the optic nerve. It is considered a developmental extension of the brain and is the only part of the CNS which can be imaged using non-invasive procedures.

Recent advances in technology have started to show us significant improvements in microvascular pathology, as a result it may lead to discovering sensitive biomarkers that help us understand cerebral processes better.

One of them being OCT Angiography development which has given us a detailed view of the measurements, shape and blood flow of the retinal capillaries in the human eye without the injection of any dyes or contrast agents.

Various studies have shown pRNFL thickness to be decreased in patients with AD. The ganglion cell layer and its axons consist of one third of the total retinal thickness of the macula and seem to be the most affected layer in AD. A meta-analysis with 30 cross-sectional studies confirmed a correlation between OCT retinal measurements such as ganglion cell-inner plexiform layer, ganglion cell complex, macular volume and thickness and choroidal, RNFL thicknesses of AD patients. Furthermore OCTa has shown reduced vascular density in macular, foveal and parafoveal zones in these patients in addition with expansion of the foveal avascular zone [2,3].

## **6.2 Optical Coherence Tomography in Multiple Sclerosis**

Edema and neurodegeneration are commonly indicated by the changes in GCIPL and the RNFL. Although this is not specific for MS. However, there are studies that push the narrative that the severity and distribution of GCIPL and RNFL along with temporal development may help us differentiate MS from other neurodegenerative diseases.

Observations are usually made after retinal arterial occlusion, which makes OCT much more useful than any dye, as they only seem to be detectable in the acute phase. In idiopathic intracranial hypertension there is usually symmetrical swelling of the optic nerve head, unlike MS which is asymmetrical.

Several studies have discovered significant reduction in the GCL thickness in the eyes of MS patients without previous history of Optic neuritis (ON) which may show subclinical structural damage. This may also suggest that it could be easier to detect patients who are at a risk of developing MS whilst still being diagnosed with Optic neuritis [4].

The correlation between the thickness of GCIPL and RNFL, and visual acuity, especially low contrast visual acuity has been shown across multiple studies. A significant correlation was also found between dyschromatopsia and GCIPL thickness in MS-NON eyes [5].

### **6.3 Optical Coherence Tomography in Parkinson's Disease**

Brain microvasculature has been a significant factor along with neurodegeneration in recent studies for the epidemiology and progression of neurodegenerative diseases. The arrival of OCTa has helped us to check noninvasively if microvascular changes in the retina can be a potential biomarker for neurodegenerative disorders including Parkinson's disease (PD). Since non-invasive tests currently are not developed for the early detection of PD, many studies have looked at the association of OCTa measurements such as retinal vascular density and foveal avascular zone (FAZ), with PD incidence rates.

The use of SMD was used as a summary analysis in this study. Due to the variations of OCTa measurements of vessel density of retinal microvasculature in different machines. This is useful as we use the same outcome but use different ways to measure it.

Several studies have shown the variants of the brain vasculature in PD like multiple system atrophy and progressive supranuclear palsy. Dopamine is an important neuromodulator of the retina which regulates multiple visual functions including, circadian nature of light-adapted vision and contrast acuity. Although the exact nature of the pathophysiology of reduced vessel density in patients with PD still remains a mystery. Certain hypotheses were put forward such as degeneration of dopamine neurons lead to the vessel fragmentation and loss of capillary connections due to the interactions of endothelial cells, neurons and glial cells, which as whole form a functional and structural unit.

An Inadequate number of screening questions for non-motor symptoms, metric inaccuracies, and non-specificity of the mentioned texts are some of the drawbacks of the UPRDS scale which are the current methods used to diagnose PD.

Results however need to be interpreted with caution, since the difference in vessel density and in patients with PD and controls for many vascular plexuses are marginal and below the levels of repeatability of vessel density measured by OCTa [6,28].

Parkinson's disease has a distinct retinal signature: They exhibit a unique form of pattern with its retinal degeneration, which is closely related to longevity of the disease and motor dysfunction. This finding shows the dopaminergic deficiency. This is because the retina contains a high concentration of dopaminergic amacrine cells [25,26].

### **6.3.1 Quantitative retinal measurements**

RNFL thinning: Studies that use spectral domain OCT (SD-OCT) typically show a reduced RNFL thickness across superior, inferior, nasal and temporal quadrants. With the degree of thinning showing a direct association with disease longevity and advancing stage of the disease. Macular and ganglion cell parameters: Quantitative measurements show notable thinning in important parameters. For example; one study showed the mean of average macular thickness with  $p = 0.021$ , inner superior macular thickness with  $p \leq 0.007$ , inner temporal macular thickness with  $p = 0.002$ , outer superior macular thickness with  $p = 0.047$ , and outer temporal macular thickness with  $p = 0.045$  in PD patients, all when in comparison to healthy controls are low [21].

Foveal and Vascular changes: Findings of foveal changes have been unclear, with studies showing foveal pit widening or non-symmetry. OCTa reveals microvascular changes in PD, those including reduced circulation in the foveal avascular zone (FAZ) and reduced vessel density.

The differential patterns of atypical Parkinsonian Syndromes: It is a huge clinical challenge to distinguish PD from APS, like progressive supranuclear palsy (PSP) and multiple system atrophy (MSA).

### **6.3.2 Progressive Supranuclear Palsy (PSP)**

PSP is associated with the most remarkable thinning seen in parkinsonian syndromes. Quantitative studies show that PSP patients show reduced values for Central macular thickness ( $p < 0.001$ ; MD:  $-85.000$ ,) and GCL–IPL complex thickness ( $p = 0.016$ , MD:  $-6.571$ ). When compared to patients who suffer from PD and MSA these values are profoundly lower. This significant reduction shows the overall neurodegeneration seen in brains with PSP [22].

### **6.3.3 Multiple system atrophy (MSA)**

It typically presents with an intermediate retinal phenotype. The severity of parameters places MSA between PD and PSP. The measurements show a central macular thickness of  $245.2 \pm 35.4$ , and GCL–IPL complex thickness of  $77.9 \pm 7.5$  [22].

#### **6.4 Optical coherence tomography in Amyotrophic lateral sclerosis**

ALS has always been grouped as a motor system disease. However, there has been increasing evidence of the involvement of nonmotor systems such as the eyes. The common embryological origin of the retinal cells and neurons of the CNS may suggest that neurodegenerative conditions that affect the brain and spinal cord may affect retinal cells as well.

There might be a correlation between retinal nerve fiber layer (RNFL) measurements and ALS. Other OCT parameters have been used to predict disease severity in patients with ALS. The abovementioned parameters include retinal layers other than RNFL, whole retinal thickness and macular thickness.

The meta-analysis in this study showed that RNFL thickness was not noteworthy of a difference with ALS patients and controls regardless of the quadrants compared. However, individually conducted studies showed notable narrowing of RNFL in ALS patients compared to controls. Trivial results were obtained for the thickness of the inner plexiform layer, outer plexiform layer, outer nuclear layer, macula, as well as for the total retinal thickness between ALS patients and controls. In ALS patients however, the INL (Inner nuclear layer) was very diminished. INIL thinning measures by OCT offer to be the next indicator of neurodegeneration in ALS. The most common progression of ALS starts with the affected area in the neurological system and spreads to the surrounding regions. Majority of the patients pass away due to respiratory failure as the disease progression worsens patient function and dependence [7,29].

#### **6.5 Optical Coherence Tomography in Patients with Friedreich's Ataxia**

Baseline macular, average peripapillary and RNFL thickness showed a significant correlation in all portions except for nasal and disease progression. Additionally visual acuity showed a correlation with average macular and RNFL thicknesses. Macular thickness also showed a significant correlation with disease longevity however that was not the case for RNFL thickness as they showed no importance.

Spearman's rank correlation test was used to analyse the relationships between OCT parameters and disease longevity. Furthermore, the relationships between OCT parameters and disease severity as quantified with SARA, and visual acuity were analysed using Pearson's correlation. A marked preference for damage to the papillo-macular bundle is associated with the traditional optic neuropathy of mitochondrial dysfunction, which has the thickest density of retinal ganglion cells (RGCs), which leads to Central vision loss and temporal pallor of the optic nerve.

Overlying clinical and pathological features which are characterised by early loss of RGCs in the papillo-macular bundle are found in Leber's hereditary optic neuropathy (LHON) and dominant optic atrophy (DOA), the most found non-syndromic mitochondrial optic neuropathies.

On the other hand, a classical mitochondrial pattern is not found in optic neuropathy observed in FRDA. In the mitochondrial disorder with a genetic defect in FXN, visual impairment and the pathological mechanism are different from LHON and DOA suggesting that the papillo-macular axonal system is not involved in the process. The mitochondrial respiratory chain complexes contain an assembly of iron-sulphur clusters. Frataxin, which is an encoded mitochondrial protein, is directed to the mitochondrial inner membrane which is involved in the assembly of these clusters.

There was another correlation between RNFL thickness and disability as quantified with SARA, showing that disease progression and worsening of neurological function was seen with lower RNFL values [8].

## **6.6 Optical coherence tomography in adult adrenoleukodystrophy**

OCT can show retinal irregularities which are significantly present in adult patients suffering with adrenoleukodystrophy. These are found the most in those with parieto occipital WM lesions. Change in OCT parameters might be sensitive to the inferior pRNFL, average mGCC and inner macula thickness values, which are to be investigated more as they have exceptional utility and consistency in longitudinal studies [9].

In this particular cross-sectional study, OCT reveals that the myelopathy of ALD is associated with thinning of the retinal nerve fiber layer. Axonal degeneration with narrowing of the spinal cord has been shown in patients with ALD. When compared to controls this axonal degeneration is also measured, furthermore clinical outcome measurements of myelopathy correlate with retinal neurodegeneration.

Retinal neurodegeneration has been studied in several diseases, but a study of such kind has never been conducted for ALD. The needed initial steps in the recognition of OCT as a valued measure for myelopathy in ALD include proving a correlation between retinal neurodegeneration in ALD and clinical measures of severity of myelopathy. Neuro-retinal narrowing was observed in female patients with ALD; however, it was less noteworthy compared to the clinical outcome measures in men. The difference in disease prognosis in men

and women can probably answer this, as women have a milder course of disease, at an increased age and slower progression. In the men's subgroup the total differences in retinal layer thickness were highest for the pRNFL (temporal and superior quadrant), although incidence importance leaned towards RNFL. This is probably due to the bigger standard deviations of the measurements taken from pRNFL when put next to RNFL [10].

### **6.7 Study of Enhanced Depth Imaging Optical Coherence Tomography in Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy.**

SFCT was to be evaluated because it is highly replicable and it is widely used in other small-vessel illnesses. The present study reveals reduced SFCT in CADASIL patients. Young adults with hypertension had majorly lower SFCT levels compared to healthy individuals. Thinner SFCT was also observed in diabetic patients without diabetic retinopathy and in patients with migraine. Ocular ischemic syndrome was also seen to be associated with a decrease in mean SFCT.

It was later confirmed through the study that the outer diameter of arteries and veins were much thicker than those in healthy controls. Since the walls of the vessels are much thicker in arteries and veins. The inner diameter of arteries in patients with CADASIL was notably lower and which led to a narrowed arterial lumen. Luminal stenosis caused by arterial wall thickening is a finding consistent in characterization of CADASIL by a pathological study. Similar measures of outer diameters and vessel wall in arteries and veins were reported in CADASIL patients. They also found no noteworthy difference in inner arterial diameter between CADASIL patients and healthy controls.

EDI-OCT examination was used to confirm the decrease in SFCT and retinal artery lumina in Chinese CADASIL patients. In these patients there were increased values of retinal artery outer diameter, venous inner, outer diameter and vessel wall thickness of both the veins and arteries. Tapering of the retinal arterial lumen is related to infarcts and widening of veins related to CMBs. EDI-OCT is a useful diagnostic tool for CADASIL follow-up patients with the measurements of retinal vessels [11].

### **7. Limitations of OCT and OCTa**

OCTa was first used in 2015, and most of the data comes from small studies with small sample sizes, this limits the proof available and questions the validity of the findings. A learning curve

is present when brought into interpretation as there is no single protocol developed to take which values into account. This may lead to errors such as false-positive or -negative results which are misleading and can be contradictory to the available studies [1].

Another noteworthy limitation would include the extent to which the patients cooperate for an OCTa image whilst suffering from neurodegenerative diseases. As a result, this may lead to lower quality images being obtained and cause inaccurate reading of the images due to motion factors. Since OCT and OCTa demand high patient cooperation and attention, it may not be the best option for children and those who are easily irritated taking their condition into consideration. Many of these patients may also be geriatric and have conditions such as hypertensive retinopathy, diabetic retinopathy, primary open-angle glaucoma, vein occlusions and macular degeneration which can alter OCT measurements as they may be non-specific.

Non-specificity of findings is another drawback. Retinal thinning, especially that of the RNFL is a reoccurring finding in many different pathologies including glaucoma, diabetic retinopathy and healthy ageing. In cases where patients have ocular or systemic conditions, the non-specificity of these parameters complicates the interpretation of OCT readings [1,19].

Having no guidelines or standardizations yet as they are not actively researched about is something that should be worked towards achieving [24].

## **8. Discussion**

Over the last few years there has been a lot of interest in OCT in the field of neurodegenerative illnesses. Considering it is easily accessible and minimally invasive, the use of OCT to find biomarkers will have an outstanding impact on the general population for neurodegenerative population screening. There is also the plausibility of prevention of neurodegeneration along with clinical application of OCT in examining the therapeutic administration of certain drugs on ocular parameters.

OCT findings should be set alongside other established biomarkers to improve the accuracy of diagnosis. Future studies should be able to correlate retinal parameters with neuroimaging, cerebrospinal fluid biomarkers and genetic risk factors with in-depth clinical assessment.

Artificial intelligence and machine learning technologies may help in automated image analysis, pattern recognition as well as monitoring drug efficiency. These tools could help us identify disease specific variations from very complicated data and alter further treatment plans of these diseases [20,23,30].

## 9. Conclusions

Numerous studies show that retinal parameters show a correlation with neurodegenerative diseases. Evidence suggests that retinal thinning, microvascular alterations, and changes in retinal perfusion may serve as early detectors of the disease, its progression and severity. These findings potentially provide a safe and minimally invasive pathway to explore neurodegenerative pathology.

Despite promising results, several limitations hold back OCT and OCTa use in neurology. Many of the studies have small sample sizes and lack a proper protocol to be followed. Furthermore, findings such as RNFL thickness seem to be non-specific and complicates interpretation. Future research should focus on large scale longitudinal studies. Integration of other factors such as neuroimaging, cerebrospinal fluid markers and the use of artificial intelligence may enhance this unexplored field of neuro-ophthalmology.

### Disclosure

Authors do not report any disclosures

### Author's Contribution

Conceptualization: Agata Król

Methodology: Agata Król, Edyta Lewandowska, Emilia Muraszewska, Łukasz Muraszewski, Eryk Ubysz, Patrycja Kwitowska, Małgorzata Pyjecka, Cezary Łuczyński, Mariusz Wręczycki, Maciej Paczkowski

Resources: Łukasz Muraszewski, Cezary Łuczyński, Maciej Paczkowski, Edyta Lewandowska

Data curation: Mariusz Wręczycki, Małgorzata Pyjecka, Maciej Paczkowski

Formal analysis: Agata Król, Patrycja Kwitowska, Eryk Ubysz, Mariusz Wręczycki

Investigation: Agata Król, Cezary Łuczyński, Patrycja Kwitowska, Edyta Lewandowska

Supervision: Eryk Ubysz, Małgorzata Pyjecka, Emilia Muraszewska

Writing-rough preparation: Agata Król, Emilia Muraszewska, Łukasz Muraszewski, Patrycja Kwitowska, Eryk Ubysz, Edyta Lewandowska, Mariusz Wręczycki

Writing-review and editing: Agata Król, Małgorzata Pyjecka, Emilia Muraszewska, Łukasz Muraszewski, Cezary Łuczyński, Maciej Paczkowski

All authors have read and agreed with the published version of the manuscript.

Funding Statement:

This research received no external funding.

Institutional Review Board Statement:

Not applicable.

Informed Consent Statement:

Not applicable.

Data Availability Statement:

Not applicable.

Acknowledgments:

Not applicable.

Conflict of Interest Statement:

The authors declare no conflict of interest.

## References

1. Tsokolas G , Tsaousis KT , Diakonis VF , Matsou A , Tyradellis S. Optical Coherence Tomography Angiography in Neurodegenerative Diseases: A Review. *Eye Brain*. 2020;12:73–87. <https://doi.org/10.2147/EB.S193026>
2. Cunha LP, Pires LA , Cruzeiro MM, Almeida ALM, Martins LC, Martins PN, Shigaeff N, Vale TC. *Arq Neuropsiquiatr*. 2022;80(2):180-191. <https://doi.org/10.1590/0004-282X-ANP-2021-0134>
3. Katsimpris A, Karamaounas A, Sideri AM, Katsimpris J, Georgalas I, Petrou P. Optical coherence tomography angiography in Alzheimer's disease: a systematic review and meta-analysis. *Eye (Lond)*. 2022;36(7):1419-1426. <https://doi.org/10.1038/s41433-021-01648-1>
4. Britze J, Frederiksen JL. Optical coherence tomography in multiple sclerosis. *Eye (Lond)*. 2018;32(5):884-888. <https://doi.org/10.1038/s41433-017-0010-2>
5. Lampert EJ, Andorra M, Torres-Torres R, Ortiz-Pérez S, Llufríu S, Sepúlveda M, Sola N, Saiz A, Sánchez-Dalmau B, Villoslada P, Martínez-Lapiscina EH. Color vision impairment in multiple sclerosis points to retinal ganglion cell damage. *J Neurol*. 2015;262(11):2491-7. <https://doi.org/10.1007/s00415-015-7876-3>
6. Katsimpris A, Papadopoulos I, Voulgari N, Kandarakis S, Petrou P, Karampitsakos T, Dimitropoulou AN, Katsimpras M, Karamaounas A, Sideri AM, Katsimpris J, Georgalas I, Kymionis G. Optical coherence tomography angiography in Parkinson's disease: a

- systematic review and meta-analysis. *Eye (Lond)*. 2023;37(14):2847-2854. <https://doi.org/10.1038/s41433-023-02438-7>
7. Nepal G, Kharel S, Coghlan MA, Yadav JK, Parajuli P, Pandit K, Shing YK, Ojha R. Amyotrophic lateral sclerosis and retinal changes in optical coherence tomography: A systematic review and meta-analysis. *Brain Behav*. 2022;12(9):e2741. <https://doi.org/10.1002/brb3.2741>
  8. Bogdanova-Mihaylova P, Plapp HM, Chen H, Early A, Cassidy L, Walsh RA, Murphy SM. Longitudinal Assessment Using Optical Coherence Tomography in Patients with Friedreich's Ataxia. *Tomography*. 2021;7(4):915-931. <https://doi.org/10.3390/tomography7040076>
  9. Bianchi-Marzoli S, Fenu S, Melzi L, Benzoni C, Antonazzo F, Tomas Roldan E, Farina L, Tremolada G, Mauro E, Pensato V, Gellera C, Pareyson D, Salsano E. Optical coherence tomography in adult adrenoleukodystrophy: a cross-sectional and longitudinal study. *Neurol Sci*. 2021;42(1):235-241. <https://doi.org/10.1007/s10072-020-04576-2>
  10. van Ballegoij WJC, Kuijpers SC, Huffnagel IC, Weinstein HC, Poll-The BT, Engelen M, Bennebroek CAM, Verbraak FD. Optical coherence tomography shows neuroretinal thinning in myelopathy of adrenoleukodystrophy. *J Neurol*. 2020;267(3):679-687. <https://doi.org/10.1007/s00415-019-09627-z>
  11. Fang XJ, Yu M, Wu Y, Zhang ZH, Wang WW, Wang ZX, Yuan Y. Study of Enhanced Depth Imaging Optical Coherence Tomography in Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy. *Chin Med J (Engl)*. 2017;130(9):1042-1048. <https://doi.org/10.4103/0366-6999.204935>
  12. Pandya BU, Grinton M, Mandelcorn ED, Felfeli T. RETINAL OPTICAL COHERENCE TOMOGRAPHY IMAGING BIOMARKERS: A Review of the Literature. *Retina*. 2024;44(3):369-380. <https://doi.org/10.1097/IAE.0000000000003974>
  13. López-Cuenca I, de Hoz R, Alcántara-Rey C, Salobrar-García E, Elvira-Hurtado L, Fernández-Albarral JA, Barabash A, Ramírez-Toraño F, de Frutos-Lucas J, Salazar JJ, Ramírez AI, Ramírez JM. Foveal Avascular Zone and Choroidal Thickness Are Decreased in Subjects with Hard Drusen and without High Genetic Risk of Developing Alzheimer's Disease. *Biomedicines*. 2021;9(6):638. <https://doi.org/10.3390/biomedicines9060638>

14. Chalkias E, Chalkias IN, Bakirtzis C, Messinis L, Nasios G, Ioannidis P, Pirounides D. Differentiating Degenerative from Vascular Dementia with the Help of Optical Coherence Tomography Angiography Biomarkers. *Healthcare (Basel)*. 2022;10(3):539. <https://doi.org/10.3390/healthcare10030539>
15. Yoon JM, Lim CY, Noh H, Nam SW, Jun SY, Kim MJ, Song MY, Jang H, Kim HJ, Seo SW, Na DL, Chung MJ, Ham DI, Kim K. Enhancing foveal avascular zone analysis for Alzheimer's diagnosis with AI segmentation and machine learning using multiple radiomic features. *Sci Rep*. 2024;14(1):1841. <https://doi.org/10.1038/s41598-024-51612-8>
16. Salobar-Garcia E, Méndez-Hernández C, Hoz R, Ramírez AI, López-Cuenca I, Fernández-Albarral JA, Rojas P, Wang S, García-Feijoo J, Gil P, Salazar JJ, Ramírez JM. Ocular Vascular Changes in Mild Alzheimer's Disease Patients: Foveal Avascular Zone, Choroidal Thickness, and ONH Hemoglobin Analysis. *J Pers Med*. 2020;10(4):231. <https://doi.org/10.3390/jpm10040231>
17. Liu WW, Margeta MA. Imaging Retinal Ganglion Cell Death and Dysfunction in Glaucoma. *Int Ophthalmol Clin*. 2019;59(4):41-54. <https://doi.org/10.1097/IIO.0000000000000285>
18. Mutlu U, Ikram MK, Roshchupkin GV, Bonnemaier PWM, Colijn JM, Vingerling JR, Niessen WJ, Ikram MA, Klaver CCW, Vernooij MW. Thinner retinal layers are associated with changes in the visual pathway: A population-based study. *Hum Brain Mapp*. 2018;39(11):4290-4301. <https://doi.org/10.1002/hbm.24246>
19. Dhirachaikulpanich D, Chanthongdee K, Zheng Y, Beare NAV. A systematic review of OCT and OCT angiography in retinal vasculitis. *J Ophthalmic Inflamm Infect*. 2023;13(1):1. <https://doi.org/10.1186/s12348-023-00327-4>
20. Meng Z, He Y, Guo K, Li L. Imaging biomarkers in optic neuritis: current tools and future directions. *Front Neurol*. 2025;16:1666835. <https://doi.org/10.3389/fneur.2025.1666835>
21. Abd Hamid MR, Wan Hitam WH, Abd Halim S. Retinal Nerve Fiber Layer and Macular Thickness in Parkinson's Disease Patients. *Cureus*. 2021;13(7):e16224. <https://doi.org/10.7759/cureus.16224>
22. Svetel M, Marić G, Božić M, Pekmezović T, Petrović I, Jakšić J, Dimitrijević A, Lazić U, Kostić S, Knežević M, Petrović T, Pajić SP, Šobot V, Vasiljević J, Svetel M. Retinal Thickness Profiles in Parkinsonian Syndromes: Discerning Parkinson's Disease, Multiple

- System Atrophy, and Progressive Supranuclear Palsy via Optical Coherence Tomography. *Biomedicines*. 2026;14(1):249. doi: <https://doi.org/10.3390/biomedicines14010249>
23. Jessney B, Chen X, Gu S, Huang Y, Goddard M, Brown A, Obaid D, Mahmoudi M, Garcia Garcia HM, Hoole SP, Räber L, Prati F, Schönlieb CB, Roberts M, Bennett M. Artificial Intelligence-Led Whole Coronary Artery OCT Analysis; Validation and Identification of Drug Efficacy and Higher-Risk Plaques. *Circ Cardiovasc Imaging*. 2025;18(11):e018133. <https://doi.org/10.1161/CIRCIMAGING.125.018133>.
  24. Reeß LG, Salih H, Delikaya M, Paul F, Oertel FC. Barriers in Healthcare to the Use of Optical Coherence Tomography Angiography in Multiple Sclerosis. *Neurol Ther*. 2025;14(1):45-56. <https://doi.org/10.1007/s40120-024-00670-1>
  25. Ueda E, Watanabe M, Nakamura D, Matsuse D, Tanaka E, Fujiwara K, Hashimoto S, Nakamura S, Isobe N, Sonoda KH. Distinct retinal reflectance spectra from retinal hyperspectral imaging in Parkinson's disease. *J Neurol Sci*. 2024;461:123061. <https://doi.org/10.1016/j.jns.2024.123061>
  26. Ortuño-Lizarán I, Sánchez-Sáez X, Lax P, Serrano GE, Beach TG, Adler CH, Cuenca N. Dopaminergic Retinal Cell Loss and Visual Dysfunction in Parkinson Disease. *Ann Neurol*. 2020;88(5):893-906. <https://doi.org/10.1002/ana.25897>
  27. 2025 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2025;21(4):e70235. <https://doi.org/10.1002/alz.70235>
  28. Giachos I, Doumazos S, Tsiogka A, Manoli K, Tagaris G, Rotsos T, Kozobolis V, Iliopoulos I, Moschos M. Retinal capillary plexus in Parkinson's disease using optical coherence tomography angiography. *Int J Ophthalmol*. 2024;17(1):131-136. <https://doi.org/10.18240/ijo.2024.01.18>
  29. Pang C, Li Y, Jiang W, Xie H, Cao W, Yu H, Lin Z, Cheng Y, Fan D, Deng B. Analysis of retinal markers and incident amyotrophic lateral sclerosis: An optical coherence tomography-based cohort study. *PLoS Med*. 2025;22(6):e1004545. <https://doi.org/10.1371/journal.pmed.1004545>
  30. Zhao Y, Xiao Q, Fan B, Tang L, Chen X, Dai Y. Multimodal optical coherence tomography and angiography and serologic markers for accurate early diagnosis of dysthyroid optic neuropathy. *Am J Transl Res*. 2026;18(1):676-690. <https://doi.org/10.62347/SDKT8956>

31. Vujosevic S, Parra MM, Hartnett ME, O'Toole L, Nuzzi A, Limoli C, Villani E, Nucci P. Optical coherence tomography as retinal imaging biomarker of neuroinflammation/neurodegeneration in systemic disorders in adults and children. *Eye (Lond)*. 2023;37(2):203-219. <https://doi.org/10.1038/s41433-022-02056-9>