Summary:

Multiple sclerosis (MS) is an autoimmune disease of the nervous system that leads to degeneration of this system. It has multiple potential etiologies and is characterized by autoimmune pathogenesis. The disease is characterized by progressive neurodegeneration, which results in damage to motor neurons and can also affect other systems, including the visual organs.

Depending on the specific subtype of the disease, it can exhibit either a very fast or slow progression, leading to limitations in the patient's mobility. Visual organs are frequently affected, which further complicates the functioning of the patients.

A significant majority of individuals with multiple sclerosis (MS) experience visual disturbances, either associated or not with optic neuritis. As the disease progresses, irreversible vision loss can occur, which, combined with physical disabilities, leads to the inability to function effectively in their environment, resulting in the isolation of the patient. This hastens the complete social disconnection of the patient from their social life and the ability to perform basic daily activities. Therefore, analyzing the morphological parameters of the eye's retina allows for the interpretation of the quality of impairments, their progression over time, and the identification of new biomarkers for monitoring disease progression and treatment.

Until now, a comprehensive analysis of the morphological parameters of the eye's retina in patients with MS has not been undertaken, compared to a control group, using new technologies such as rtx1 and OCT. It is crucial to attempt to systematize the retinal changes in individuals with MS who have experienced visual disturbances, including optic neuritis (ON), and those who have not. Undertaking these actions is important and justified because their results will help identify new biomarkers of disease progression and potential treatments, such as stem cell transplantation, which could improve the morphological parameters of the retina, visual acuity, and enhance the overall quality of life for patients.

The main objective of the doctoral thesis was to conduct a thorough analysis of the morphological parameters of the retina in individuals with multiple sclerosis, with a specific emphasis on photoreceptor cells known as cones. These cells play a crucial role in capturing visual stimuli from the external environment. Additionally, the study investigated other parameters that could offer insights into the non-invasive monitoring of the disease's progression, even though multiple sclerosis affects the entire body.

The participants in my research group consisted of individuals burdened with multiple sclerosis, specifically focusing on studying the morphological changes in the retina during the course of the disease. The average age of the 34 persons in the control group was 36.5 ± 11.1 years, while in the group of 43 patients with multiple sclerosis, it was 40.2 ± 9.83 years. This age range aligns with the typical age of onset for the diagnosis of MS. Among the participants in the study group, 70% were women. The composition of the study group was similar to that described in scientific studies and included individuals participating in therapeutic programs conducted by neurologists. Consequently, it can be stated that the study group in which my research was conducted was suitable for comparing the morphological parameters of the eye's retina between individuals with MS(+) and the control group. The study group included patients at various stages of the disease over the course of its duration.

The patients underwent non-invasive examinations using the devices mentioned in the methodology. Between individual examinations, no new neurological or ophthalmic diseases were diagnosed in the participants. Additionally, in the case of patients with multiple sclerosis, there were no occurrences of relapses during the study.

In the assessment of parameters using OCT Spectralis, the following measurements were taken in both eyes: average retinal thickness in the fovea using cross-sectional measurement, averaged retinal thickness values in the fovea within a 1mm circle encompassing the fovea, averaged thickness values of the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner nuclear layer (INL), and photoreceptors within a 3mm circle encompassing the fovea, divided into upper, lower, temporal, and nasal segments. Values below or above those standardized in the device were considered abnormal. Analyses were conducted between the groups of MS (+) and MS (-), MS (+) without visual disturbances and MS (-), MS (+) with visual disturbances and MS (-), as well as between MS (+) with visual disturbances and MS (+) without visual disturbances.

In the assessment of parameters using rtx1 - AORC, measurements were taken in both eyes for the cones in the fovea at depths ensuring the best sharpness of the displayed image. These measurements were divided into upper, lower, temporal, and nasal segments. Additionally, the upper temporal artery was examined to obtain values such as outer and inner vessel diameter, vessel wall thickness, calculated vessel wall thickness to inner vessel diameter ratio, and vessel wall surface area in cross-sectional view. All these values were compared between the group of individuals with multiple sclerosis and the control group. Comparative analyses were conducted between various subgroups, including individuals with multiple

sclerosis (SM+), the control group, individuals with multiple sclerosis without visual disturbances (SM+ without visual disturbances) and the control group, as well as between individuals with multiple sclerosis with visual disturbances (SM+ with visual disturbances) and those without visual disturbances (SM+ without visual disturbances).

For the assessment of clinical parameters, values of peripheral arterial blood pressure were measured in the brachial artery and central aorta, including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP), and heart rate (HR). Additionally, parameters related to the elasticity of large blood vessels and the pulse wave velocity between the common carotid artery and the femoral artery were measured.

For the evaluation of parameters in the common right and left carotid arteries, measurements were taken for Intima-Media Thickness (IMT), inner diameter (LT), and Intima-Media Thickness Lumen Ratio (IMTLR), 2 centimeters below the bifurcation of the common carotid artery during diastole.

The results of the conducted research analyzing the morphological parameters of the eye's retina indicate that in patients with multiple sclerosis, there are no changes in the photoreceptor layer despite existing changes in other layers of the retina. The observed alterations in the internal and external diameters of the upper temporal arteries in the retina did not influence the number of examined cones, but rather were the result of neurodegenerative changes occurring in other retinal layers. A parameter that could potentially indicate functional changes in cones could be their shape (regularity) rather than their quantity, but this would require studies on a homogeneously large group of patients, especially those diagnosed at an advanced stage of multiple sclerosis.

The study also demonstrated that certain parameters measurable in OCT Spectralis, primarily related to ganglion cell layer and axons, could serve as biomarkers of disease activity and treatment effectiveness, as similarly reported in literature.

These findings allow for the postulation that appropriate types of treatment (e.g., using stem cells) may have a chance to halt neurodegenerative changes in multiple sclerosis, provided that effective therapies are implemented promptly before inflammatory states of the optic nerve axons lead to the death of ganglion cells. The observed lack of significant deficits in the

photoreceptor and inner nuclear layers in the early years after diagnosis offers hope that stopping the neurodegeneration of the third neuron of the visual pathway provides an opportunity to preserve the entire afferent visual pathway, provided appropriate therapy is administered.