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**“ASSESSMENT OF RETINAL
MICROCIRCULATION PARAMETERS IN
PRIMARY OPEN ANGLE GLAUCOMA
USING ADAPTIVE OPTICS TECHNOLOGY”**

**Rozprawa na stopień doktora nauk medycznych i nauk o
zdrowiu w dyscyplinie nauki medyczne**

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[SUMMARY]

Glaucoma is a neurodegenerative group of diseases characterised by degeneration of ganglion cells and its axons, which results in damage to the optic nerve and permanent visual field loss. Glaucoma is the leading cause of irreversible blindness worldwide [1] and occurs with a frequency of about 3.4 per cent amongst people aged 40-80 years [2]. Primary open-angle glaucoma (POAG) is the most common type of glaucoma and represents around 75 % of all cases of the disease [3]. POAG is characterized by a complex multifactorial pathogenesis and a usually asymptomatic course in the early stages, which makes it a great challenge for modern medicine. To prevent blindness and improve disease control, it is necessary to understand the pathophysiological mechanisms and markers of disease progression. Therefore, the use of new technologies and diagnostic methods is crucial in POAG. Among them, a promising technology is adaptive optics (AO), the first method that allows previously unachievable analysis of eye structures at the cellular level in vivo, and thus a more accurate understanding of POAG.

The aim of this dissertation, based on a series of three publications, is to assess the vascular changes in the retinal microcirculation in patients with POAG and to evaluate the correlation of the severity of vascular changes with the progression of POAG using the AO technique. In addition, this dissertation analyses recent developments in the diagnosis and monitoring of glaucoma with particular emphasis on the role of AO.

The first article composing the publication series, a narrative review article, presents, in accordance with current medical knowledge, the latest findings and publications on the recent developments in the diagnosis and monitoring of glaucoma. Firstly, the development of tonometry is described, as intraocular pressure (IOP) is the only factor that can be modified with treatment. Technologies that make the use of fundus cameras (FC) in optic nerve evaluation with its documentation easier and more widespread are discussed. The publication also broadly describes the evolution of optical coherence tomography (OCT) in terms of image quality, imaging protocols and new parameters. The most important test to assess the degree of functional glaucomatous damage is perimetry. The publication presents new developments including perimetry with fundus tracking, combined structure function index (CSFI), novel perimetry algorithms and improved analytical techniques. The publication also presents the application of different types of visual electrophysiological tests and their modifications, which can be a useful additional tool to conventional tests in glaucoma. The paper highlights the role of artificial intelligence (AI) in the diagnosis and monitoring of glaucoma. The application of

AI in glaucoma for the assessment of structural changes (such as fundus photographs, OCT) and functional changes (perimetry) as well as for the prognosis of patients with glaucoma is presented. In addition, the article describes the appliance of AO in the diagnosis and monitoring of glaucoma.

The second paper is also a review article, which summarises the application of AO technology in ophthalmology. The article reviews the principles of AO and the types of AO used in ophthalmology. AO alone cannot produce an image, so the AO system must be integrated with existing retinal imaging devices such as FC, scanning laser ophthalmoscopy (SLO) and OCT. This article summarises, in accordance with current medical knowledge, the available studies and publications in the literature concerning the use of AO in a number of disease entities, including diabetic retinopathy, age-related macular degeneration, hypertensive retinopathy, glaucoma, central serous chorioretinopathy, retinal dystrophies, inflammatory diseases.

The third publication is an original article describing a study conducted as part of a dissertation research procedure at the Public Clinical Ophthalmic Hospital in Warsaw. The study aimed to assess temporal retinal arteriolar parameters in patients with POAG at different stages of progression using the adaptive optics fundus camera (AO-FC) Rtx1™ (Imagine Eyes, Orsay, France; version 3.4 – AO Image 3.4), the first commercially available device integrated with AO. Secondly, we wanted to investigate correlations between vascular parameters and glaucoma severity that were determined by structural changes on OCT (retinal nerve fibre layer (RNFL), ganglion cell complex (GCC) and rim area) and functional changes in perimetry (mean deviation (MD), pattern standard deviation (PSD)). Furthermore, we wanted to compare retinal vascular parameters in glaucoma patients to a healthy group. The study included 111 eyes of 58 patients diagnosed and treated with POAG for at least two years from the Glaucoma Outpatient Clinic and 70 eyes of 38 healthy volunteers. The study group was divided into three subgroups according to glaucoma severity: group A – preperimetric glaucoma (37 eyes); group B – early perimetric glaucoma according to the criteria of the simplified Hodapp classification (48 eyes); group C – moderate perimetric glaucoma according to the criteria of the simplified Hodapp classification (26 eyes) [4]. The control group consisted of healthy subjects, age-matched to the study groups. All subjects had to meet strict eligibility criteria and be matched for age, sex, blood pressure, and body mass index (BMI) to ensure that the above-mentioned factors did not affect the reliability of the results. Using the AO-FC Rtx1™, the following parameters of the superior and inferior temporal retinal arterioles were measured at a distance of 0.5-1 disc diameter from the edge of the optic disc: total diameter (TD), vessel wall thickness (WT), lumen diameter (LD), the wall-to-lumen ratio (WLR) and the wall cross-sectional area

(WCSA). In the statistical analysis $p < 0.05$ was taken as the level of significance. The study showed significantly lower TD and LD values and higher WLR and WT values for the superior and inferior temporal arterioles in all groups with POAG compared to the control group. In addition, TD was significantly positively correlated with RNFL and GCC thickness. LD was significantly positively correlated with RNFL, GCC and rim area. WLR was significantly negatively correlated with RNFL, GCC, rim area and MD, while it was significantly positively correlated with cup to disc ratio (CDR) and PSD. In contrast, no statistically significant differences were observed for the parameter WCSA between the groups with POAG and the control group, which may indicate eutrophic vascular remodelling, characterised by increased WLR and unchanged WCSA.

Summarising, this study has demonstrated that retinal arteriolar changes are indeed present in POAG, even at a very early stage of the disease, and correlate with the progression of glaucomatous changes. To our knowledge, this study is the first attempt to analyse retinal vascular morphology using AO in correlation with structural and functional tests in POAG. This study may provide better insight into the pathogenesis and progression of glaucoma, and thus may contribute to better diagnosis and treatment of the disease.