

OPINION

From: **Assoc. Prof. Kalina Zlatkova Trifonova-Slaveykova, MD, PHD**

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Based on Order No. 109-184/08.04.25 by the Rector of the Medical University –
Varna

Regarding: the dissertation of **Dr. Vladislava Nikolaeva Yotsova**, PhD student in full-time education, at the Department of "Eye Diseases and Visual Sciences" at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, on the topic: **"Current Diagnostic Options for Fuchs' Endothelial Dystrophy"**, for obtaining the educational and scientific degree "Doctor" in the scientific specialty "Ophthalmology", professional field 7.1 "Medicine", field of higher education 7. Health Care and Sports, with scientific supervisor **Corr. Member Prof. Dr. Hristina Nikolova Grupcheva, MD, DSc, FEBO, FICO (Hon), FBCLA, FIACLE**.

Information about the PhD Candidate: Dr. Vladislava Nikolaeva Yotsova completed her secondary education at the Ekzarh Yosif High School of Foreign Languages in Razgrad in 2007. In 2013, she received her medical degree from the Medical University in Pleven. In 2018, she became a specialist in "Ophthalmology" at the Medical University in Varna. Since 2019, she has been a working physician at the University Specialized Hospital for Active Treatment of Eye Diseases – Varna. Since 2020, she has been a teaching assistant in the Department of "Medical Optics." Additionally, between 2014 and 2020, she worked at Joy Optics. Since 2020, Dr. Yotsova has been a full-time PhD student in the Department of "Eye Diseases and Visual Sciences" at the Medical University in Varna. Dr. Yotsova continuously enhances her qualifications by attending numerous courses and congresses. During her PhD studies, she conducted practical classes for students of medicine and dental medicine. She has excellent English skills and basic knowledge of German. She has also excellent computer skills.

Dissertation Structure and Formatting: The dissertation consists of 179 standard pages and includes 43 figures and 34 tables. The references include 217 sources, 2 in Cyrillic and 215 in Latin script. The dissertation includes the following sections: list of abbreviations (2 pages), figures (3 pages), tables (3 pages), summaries in Bulgarian and English, introduction (5 pages), literature review (44 pages), aims and objectives (1 page), materials and methods (17 pages),

results (41 pages), discussion (22 pages), summary (2 pages), conclusions and contributions. This structure includes all necessary components and meets the formal requirements for formatting, length, and content.

Relevance of the Topic: Dr. Vladislava Yotsova examines the most current methods for diagnosing and monitoring patients with Fuchs' endothelial dystrophy (FECD). Each method has its advantages and disadvantages, with the main drawback of specular microscopy being its limited applicability in advanced cases with reduced corneal transparency. Comparing both methods provides a more comprehensive assessment of patients' conditions. The high prevalence of this disease in the aging population, along with the increased incidence of cataracts in patients with Fuchs', highlights the need for enhanced screening prior to cataract surgery.

Literature Review: The literature review is thorough and engaging. Numerous adapted figures and tables contribute to a clearer understanding of the topic. All current methods for diagnosing and treating Fuchs' dystrophy are discussed, along with the risk factors and pathophysiology of the disease. Innovations are considered both in pharmaceutical treatments—such as hyperosmotic contact lenses—and surgical approaches, including Hemi-DMEK, regenerative treatment with ROCK inhibitors, and tissue engineering.

Research Objective: The objective of Dr. Yotsova's research is to analyze and evaluate the topographic and microstructural parameters of the cornea in patients with varying degrees of Fuchs' endothelial dystrophy, using Pentacam Scheimpflug tomography and specular microscopy. The objective is clearly defined and supported by five specific tasks.

Study Details: The study was conducted at the University Specialized Hospital for Active Treatment of Eye Diseases – Varna, between May 2023 and December 2024. It was approved by the Ethics Committee of the Medical University – Varna, Protocol No. 130/20.04.2023. All patients or their legal representatives provided informed consent after being informed about the purpose and methods of the study. All procedures complied with Good Clinical Practice and the ethical standards of the World Medical Association. Patient selection was based on clearly defined criteria, and the sample size was appropriate considering the disease's prevalence.

A total of 89 individuals were examined, 58 women (65.17%) and 31 men (34.83%). Patients were divided into two groups:

- **Group I (Control):** 42 patients (84 eyes) with no signs of Fuchs' dystrophy.
 - **Group II:** 47 individuals (94 eyes) with diagnosed Fuchs' endothelial dystrophy.
- Each group was further subdivided by 10-year age intervals.

Following the collection of medical and family history, all subjects underwent comprehensive ophthalmological examinations, including best-corrected visual acuity, intraocular pressure measurement, biomicroscopy, fundus examination, specular microscopy, and corneal tomography. The instruments used were the Nidek CEM-530 specular microscope and Pentacam HR Oculus tomograph.

Each participant was thoroughly interviewed regarding subjective and objective ocular complaints, prior illnesses or trauma, treatments (medical or surgical), history of glaucoma, use of contact lenses, and systemic diseases with their duration and therapies. The data was collected

using a questionnaire specifically developed for patients with Fuchs' endothelial corneal dystrophy.

Statistical Methods: The statistical methods for data analysis are well selected using descriptive analysis, Independent-Samples T-test, Paired-Samples T-test, and One-Way ANOVA. SPSS 19 was used for analysis. Results are presented in graphics and tables.

Results: All assigned tasks are completed in the results. Microstructural analysis revealed a significant reduction in corneal endothelial cell density with the progression of the disease. Densitometry confirmed that corneal backscatter increases with disease advancement. Older patients showed greater displacement of the cornea's thinnest point from the pupil center and disruption in the normal pattern of isopachs on topographic maps. The results showed that central corneal thickness alone cannot indicate disease severity in a single examination but may serve as a progression marker during follow-up.

Discussion: The discussion is well-structured, comparing the author's findings with studies from India, Iran, and China. The role of artificial intelligence was also addressed.

Key Findings and Contributions: The most valuable findings include the identification of demographic characteristics of patients with Fuchs' dystrophy in the Bulgarian population. The analysis shows that the disease is more prevalent in women, but men tend to experience more severe progression. The questionnaire revealed surprisingly low patient awareness of the disease, especially among men.

The dissertation's primary contribution is both scientific and practical. For the first time in Bulgaria, a study analyzes results from specular microscopy and Pentacam Scheimpflug tomography in Fuchs' dystrophy patients, categorized by age and gender. The comprehensive literature review and microstructural analysis of the corneal endothelium in affected patients versus healthy controls are unique in Bulgarian literature.

The only **limitation** of the study is its cross-sectional design. However, future longitudinal follow-up could transform the study into a more detailed investigation. Although more demanding, a longitudinal study would yield more precise insights into disease progression and complications.

Publications: In connection with the dissertation, Dr. Yotsova has presented two publications, and she is the sole author of one of them, thereby meeting the minimum scientometric criteria for obtaining the academic degree "Doctor."

Conclusion: This well-written PhD-thesis demonstrates that the PhD candidate possesses profound theoretical knowledge and professional skills in the scientific field of "Ophthalmology" and has shown the ability to conduct independent scientific research. Based on the above, I propose that the Scientific Jury **vote in favor** of awarding the educational and scientific degree "DOCTOR" to Dr. Vladislava Nikolaeva Yotsova, and I personally also give **my positive vote**.

Stara Zagora
20th of May 2025

Best regards:...

/Assoc. Prof. K. Trifonova/

Заличено на основание чл. 5, §1, б. „В“ от Регламент (ЕС) 2016/679
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