

OPINION

on Thesis submitter for a Degree of Doctor of Philosophy, Ph.D.
in professional field 4.1 Physical sciences, Biophysics
on defense procedure at the Faculty of Physics (FzF) of
Sofia University "St. Kliment Ohridski "(Sofia University)

The review is prepared by Assoc. Prof. Viktoria Milkova Nakova, PhD,
Institute of Physical Chemistry, Bulgarian Academy of Sciences, as a member of the scientific
jury according to Order № ПД38-575 / 03.10.2022 of the Rector of Sofia University.

**Title of the Thesis: " In vitro and in vivo Contact Lens Dewetting Investigations using
Placido Ring based Videokeratometry"**

**Author of the Thesis: Sebastian Marx, M.Sc. Optometry/ Vision Science, Dipl.-Ing. (FH)
AO, FIACLE**

I. General description of the submitted materials

1. Data on the submitted documents

Under the present procedure, the candidate Mr. Sebastian Marx has presented a Thesis and an Abstract, as well as the mandatory tables with a Reference for compliance with the minimum national requirements and the minimum requirements of Department of Physics, according to the regulations for acquiring the scientific degrees and holding academic positions at Sofia University "St. Kliment Ohridski". The candidate has also presented curriculum vitae, lists of publications, participation in scientific forums, diploma and other documents patents focused on the defense, but not include in the included

The documents submitted by the candidate fully comply with the requirements of the Law on the Protection of Scientific and Technological Research, the Rules of Procedure and the Regulations for the Acquisition of Scientific Degrees and Academic Positions at Sofia University "St. Kliment Ohridski".

2. Details of the candidate

Mr. Sebastian Marx has graduated from the OSZ Havelland School of Ophthalmic Optics (Rathenow, Germany) in 2000. In 2005, he successfully graduated from the University of Applied Sciences in Jena and obtained a Master's degree in Optometry. Since 2006 Mr. Sebastian Marks is a member of the International Association of Contact Lens Trainers, Germany. Since 2012 works at the JENVIS Research Institute, Jena, Germany and coordinates research projects and is responsible for the company's clinical studies. In parallel, Mr. Sebastian Marks is a lecturer at the University of Applied Sciences, Jena, Germany and a member of the German Standardization Committee. In 2010, Mr. Sebastian Marks, together with his research group, has received the prestigious Peter-Abel-Award of the VDCO eV (Vereinigung Deutscher Contactlinsen-Spezialisten und Optometristen e.V.) for the development of a new methodology for non-tear film research, and again in 2019, received an award for the study of Meibomian gland dysfunction.

3. General characteristics of the candidate's scientific achievements

The presented Thesis is written on 136 pages and contains 67 figures, 15 tables, 7 additional tables and figures, and 270 references cited. The dissertation includes results from five publications, one of which is in a quartile Q1 journal, two of them Q2 and one is in a journal quartile Q3.

The scientific publications included in the Thesis fully meet the minimum national requirements and the additional requirements of Sofia University "St. Kliment Ohridski" for the Degree of Doctor of Philosophy, Ph.D. in the relevant scientific field.

The scientific publications included in the dissertation do not repeat those from previous procedures.

There is no proven plagiarism in the submitted Thesis and Abstract.

The main goal of the Thesis is the development of a diagnostic methodology based on the combination of classical videokeratometry based on the Placido ring and the implementation of automatic registration and signal processing with specific, originally developed software. The dissertation describes how videokeratometry can be applied in vitro and in vivo through experimental laboratory studies on the one hand, and through clinical studies on the other.

The dissertation is structured into 7 sections. The essence of the videokeratometry method is described in the literature review section. Moreover, the types of contact lenses and

the effect of various relevant solutions to ensure their normal function; the classical methods for determining the wetting angle are also presented in the section.

The investigations on the topic of the dissertation are summarized in three studies. Each of them is described detailed – objectives, hypothesis, study design, methods, results, discussion and conclusions.

- In the first *in vivo* study (conducted in accordance with ethical principles) the time to the ring's change is evaluated. To evaluate the tear film, a five-segment grid is combined on images that have been extracted from videos, in the interblink period for different post-blink durations. The reflected Placido structure is evaluated on an experimental scale. The results are shown that the subjective evaluation method allows distinguishing degrees of tearing/drying of the tear film on the surface of the lens using videokeratoscopy based on the Placido method.

- The second *in vivo* study used a more efficient software-based approach that self-detects changes in the reflected image of the Placido ring by looking for changes in ring contours and changes in the grayscale of the images. In this way, the time for the different degrees of drying of segments of the network for analysis or the decrease of surface humidity with time (or the rate of drying) can be determined.

- The third *in vivo* study is dedicated to the simultaneous determination of contact lens drying and visual acuity. A link between poor lens wetting and the patient's visual acuity has been hypothesized.

3. Analysis of the scientific and scientific-applied achievements of the candidate related to this application.

Based on the conducted in-depth experimental research on the topic of the dissertation work, five achievements have been formed that summarize the main results obtained:

- The typical application of the Placido ring covers the assessment of corneal curvature and, as of 2009, the non-invasive determination of tear film breakup time. *This thesis expands the field of applications of the Placido ring in the evaluation of the degree of impaired wetting of contact lenses both in vivo and in vitro. As a result, the thesis summarizes the knowledge in the field of assessing the degree of wetting disruption of contact lenses* and reports original experimental results.

- In order to the clinical use of videokeratoscopy based on the Placido ring, it was necessary to create and experimentally verify a new strategy for analyzing the results. In the first phase of this thesis, *an original subjective analysis of the results obtained both in vivo and*

in vitro was introduced. In the subsequent development, the analysis of the results was fully objectified, in order to increase the reliability of the assessment of the condition of the tear film.

- A series of multiparametric studies were conducted to differentiate the degree of wetting disturbance at specific time points. Both a subjective assessment of tear film condition - from 1 to 3 - and a completely objective qualification based on the analysis of a two-dimensional grid of 192 segments were used. The application of this grid allowed the description of the wetting disruption process through the accumulation of time-dependent statistics for the segments with disrupted wetting. The dynamic characteristics of the impaired wetting curve include parameters such as the area under the impaired wetting curve (local, within 1 segment drying), and drying speed to a predetermined value. Both the point in space at which the drying process starts and the moment in time at which drying begins are also determined.

- In the Thesis, an original hardware technology was developed for the simultaneous assessment and correlation of visual acuity and degree of contact lens wetting impairment. This original innovation allowed the determination of the clinically relevant area of impaired wettability, which is directly related to the decrease in visual acuity by 1, 2 or 3 logarithmic levels.

- Many of the studies presented to date evaluating contact lens wetting fail to reach comparable conclusions when comparing *in vitro* and *in vivo* process studies. In the present Thesis, a series of experimental steps are demonstrated, allowing the comparison of laboratory findings with clinical studies, allowing a good and reproducible prediction of the wetting behavior of contact lenses *in vivo* using the data obtained *in vitro*.

The presented Thesis includes results from five publications published between 2019 and 2022 (one of the publications with quartile Q1, two of them Q2, one with a quartile Q3 journal, and one publication in an international professional journal.) Part of the obtained results was presented in two oral and two poster presentations at conferences. In all research papers, the candidate has significant participation. The candidate has indicated 9 more publications on the subject of the Thesis in refereed journals that are not included in the dissertation. The scientific publications on which the dissertation is based exceed the minimum national requirements and the additional increased requirements of the Faculty of Physics of Sofia University "St. Kliment Ohridski" for the Degree of Doctor of Philosophy, Ph.D. No plagiarism was registered in accordance with the law in the Thesis and Abstract submitted by the candidate.

4. Critical remarks and recommendations

The presented thesis is well structured. The content is well-organized and clear. The literature review (part 1) is comprehensively presented, which shows the good preparation, knowledge, and experience of the candidate on the subject. The results included in the abstract are presented in a rather short version, which, in my opinion, is a shortcoming, as it does not provide a complete presentation of the research conducted.

I have no personal impressions of the candidate, but from the CV provided and the way the research and results are presented, it can be seen that Mr. Sebastian Marks has serious experimental and clinical experience in this field.

5. Conclusion

Based on the presented Thesis, Abstract, and other materials, and also based on the analysis of the significance of the scientific and scientifically-applied achievements, I confirm that the scientific achievements meet the national requirements for the application and the relevant Regulations of the Sofia University "St. Kliment Ohridski" for the Degree of Doctor of Philosophy, Ph.D. In particular, the candidate satisfies the minimum national requirements in the professional field and no plagiarism has been found in the dissertation, abstract and scientific works submitted for the competition.

I give my positive assessment of the Thesis.

II. OVERALL CONCLUSION

Based on the above, I recommend the scientific jury to award the Degree of Doctor of Philosophy, Ph.D, in professional field 4.1 "Physical Sciences", Biophysics to Mr. Sebastian Marx.

23. 11. 2022

Reviewer:


Assoc. Prof. Viktoria Milkova Nakova, PhD