REVIEW

by Prof. Zlatka Borisova Stoyneva-Paskaleva, MD,
civil contract in Medical University - Plovdiv and Medical Faculty - St. Cl. Ohridski Sofia University, member of the scientific jury according to Order No. R-109-357/19.09.2022 of the Rector of MU - Varna and on the basis of Protocol No. 1/26.09.2022 of the first meeting of the scientific jury

REGARDING: Defense of the dissertation work of Dr. Lili Yordanova Yosifova, for awarding the educational and scientific degree "Doctor" in the field of higher education 7. "Health and sport", professional direction 7.1. "Medicine", scientific specialty "Physiotherapy, spa treatment and rehabilitation" at the Prof. Dr. Paraskev Stoyanov Medical University (MU)-Varna, on the topic "Study of the effect of high-power laser in diabetic sensorimotor neuropathy" with scientific supervisors Assoc. Dr. Evgenia Vladeva-Dimova, MD and Associate Professor Dr. Mira Siderova, MD

I. Defense procedure

The presented set of documents is in accordance with the Regulations for the acquisition of the educational and scientific degree "Doctor" in the MU - Varna.

Dr. Lili Yordanova Yosifova has gone through all the procedures provided for in the Rules for Development of the Academic Staff of MU - Varna. Protocol No. 8/09.09.2022 of the Faculty Council of the Department of "Physiotherapy, Rehabilitation, Sea Therapy and Occupational Diseases" at the MU of Varna was presented, at which a decision was made to expel the doctoral student with the right to defense. By Order No. R-109-357/19.09.2022 of the Rector of the MU - Varna on the basis of a report with Entry No. 102-2109/09.09.2022 by Prof. Dr. V. D. Nestorova, MD - Head of the department "Physiotherapy, Rehabilitation, Sea Therapy and Occupational Diseases", by the decision of the Faculty Council of the Faculty of Public Health at the MU - Varna according to Protocol No. 192/12.092022, Dr. Lili Y. Yosifova is dismissed with the right to defense - doctoral student in full-time study in the doctoral program "Physiotherapy, Spa and Rehabilitation", professional field 7.1 Medicine, enrolled with Order No. R-109-47/31.01.2020.

Copies have been provided of the Protocol dated 29.10.2021 for successfully passing a foreign language exam on the Blackboard platform with proficiency at a minimum level of B1 (CEFR) for a doctoral minimum according to Order No. P-100-642/21.09.2021 and Protocol dated 20.05.2021 for a successfully passed exam to cover the doctoral minimum in "Physical and

Rehabilitation Medicine" specialization in compliance with Order No. P-109-159/19.04.2021 of the Rector of MU-Varna.

She has the required registered profiles in ORCID ID 0000-0002-6193-3854 and Google Scholar, Internet address:

https//scholar.google.corn/citations?user=-ZlQlbIAAAAJ&hl:en&authuser=1.

The doctoral student has attached three publications related to the topic of the dissertation work.

II. Brief biographical data and career development

Dr. Lili Yordanova Yosifova was born in 1976 in the city of Ruse, where she graduated her secondary education in 1995. In 2001, she graduated as a "master" in the specialty "Medicine" at the Medical University of Pleven (Registration No. 003922/2001 city, MU – Pleven). In her quest for continuous development and improvement, Dr. Yosifova acquired a specialty in "Physical and Rehabilitation Medicine" (Certificate of Recognized Specialty No. 2993, Registration No. 015553/25.06.2010, MU - Varna), and in 2011 she passed individual training in Social Medicine and Health Management (Certificate No. 99-291/23.06.11 r., MU – Varna). She has participated in a number of qualifying thematic post-graduate courses: Laser therapy, Electrodiagnostics and electrostimulation, Postisometric relaxation, Acupuncture. She has also completed qualification courses in: Pedagogical competence, Legal framework regulating the training of doctoral students, Methodology of scientific research work, Ethics of scientific research, Statistical methods for data processing and presentation, Communication techniques and presentation skills, etc.

Dr. Yosifova's professional career began in 2002 at the General Medical School - Ruse as a resident physician at Anesthesia, Resuscitation and Intensive Care Clinic. Since 2004, she has been working as a physical and rehabilitation medicine doctor in a number of outpatient and inpatient medical facilities (Tsaritsa Joanna Hospital - Provadia EOOD, St. Marina Hospital EOOD, St. Anna Medical Center EOOD - Kamchia, Hospital for treatment, long-term treatment and rehabilitation - Varna branch of the Medical Institute - Ministry of the Interior, Medical centre "M.O.K." Ltd. She began her academic career in 2017, when after winning a competition she was appointed as an assistant to the Department of Marine Medicine, Physiotherapy and Rehabilitation at the Department of Physiotherapy, Rehabilitation, Sea Therapy and Occupational Diseases at the MU - Varna. Since 2017, Dr. Yosifova has also been appointed as a physician in Physical and Rehabilitation Medicine at the UMHAT St. Marina - Varna.

Her main professional and scientific interests are in the field of acupuncture, laser acupuncture and laser therapy.

Dr. Yosifova is fluent in written and spoken Russian and English.

She is a member of the Bulgarian Medical Union, the Association of Physical and Rehabilitation Medicine and the Program Council of the master's program "Rehabilitation, Sea Healing, Wellness and Spa", for which she is also the course leader.

III. Publications and scientific activity

Dr. Lili Yosifova is the author of 3 full-text scientific publications in Bulgarian periodicals on the problem of her dissertation work. She is the lead author of 2 and last third author of 1 of the publications, which testifies to her leading role in conducting the research, preparing the publications and presenting the scientific results in the scientific articles. The publications are in 2019 and 2022 and reflect the topicality of the subject.

IV. Structure of the dissertation

The work presented for review is structured according to the accepted standards of a dissertation for obtaining the scientific degree "Doctor". The dissertation is developed in a volume of 99 standard pages and includes: Table of contents (2 pages), Abbreviations (1 page), Relevance (3 pages), Literature review (28 pages), Objective and tasks (1 page) , Material and methods (12 pages), Own results (21 pages), Discussion (12 pages), Conclusions (1 page), Contributions (1 page), Publications related to the dissertation (1 p.), Bibliography (9 p.) and 3 Appendices (5 p.).

The bibliographic reference contains 129 sources, of which 11 are in Cyrillic and 118 are in Latin, it is up-to-date - about 40% of the cited sources are from the last decade, and 16% - from the last five years.

V. Evaluation of the relevance of the dissertation work

The significance of the presented dissertation work is predetermined by the choice of the topic - therapeutic influence of diabetic neuropathy, one of the most common complications of diabetes mellitus, which affects about 50% of patients with type 2 diabetes, a current problem not only in our country, but also in the world. Peripheral diabetic neuropathy, along with micro- and macroangiopathy, contributes to the development of trophic ulcers and diabetic neuroosteoarthropathy (Charcot's foot), late complications of diabetes mellitus, which not only increase the economic costs of treatment and disability, but carry the risk of amputation, even death. Diabetes mellitus is in fifth place as a cause of health loss in Bulgaria, mainly due to premature death. Compared to the other countries of the European Union, our country ranks

third in terms of age-standardized frequency of years of life lost due to diabetes in women and in fourth place in terms of health losses in men. The successful therapeutic intervention of diabetic neuropathy is still a significant problem today.

Laser MLS (multiwave locked system) high-power therapy combining two wavelengths (MLS-laser) is a physical factor with a proven anti-edematous, anti-inflammatory, regenerative and pain-relieving effect with a faster and longer-lasting therapeutic effect than traditional laser therapy. As a new type of therapy for the treatment of pain, inflammation and edema, there are sporadic clinical studies on the effect of MLS-laser in diabetic neuropathy in the available literature with a very limited number of participants.

The significance and relevance of the problem developed in the dissertation work in scientific and scientific-applied terms are indisputable.

VI. Literature review

The literature review impresses with the versatility and depth of the content analysis of the available literature. Many of the sources cited have been published in the last 10 years. The exposition is characterized by logical consistency, conciseness and sufficient concreteness in the presentation of the published foreign and Bulgarian experience on the problems of peripheral diabetic neuropathy and the related risk to the health and quality of life of the patients. A number of insufficiently elucidated aspects and still controversial issues are highlighted, especially regarding the timely and effective therapy of the disease with the means of pathogenetic and symptomatic treatment, as well as the challenges to pharmacological therapy. The device and mode of operation of the lasers, as well as characteristics, parameters and interaction with the biological targets of the laser radiation are comprehensively presented. Historically, application and clinical experience with low-intensity laser therapy and high-power laser (MLS laser) in diabetic sensorimotor neuropathy are presented.

The review presents the author as an excellently informed and thorough researcher with a critical mind. Dr. Yosifova was able to synthesize and summarize the vast amount of information, skilfully analyze the available specialized literary sources and present the controversial and poorly clarified issues.

The literature review shows knowledge of the essence of the problem, evaluates literary data creatively and critically, which allows Dr. Yosifova to formulate, in accordance with modern scientific research in this direction, a clear scientifically based goal of her work, namely: "To study the effect of high-power laser (MLS - laser) in diabetic sensorimotor polyneuropathy and to create its own work protocol".

The tasks are specific and realistic. They are well defined and adequate to solve the set goal, namely: the impact of high-energy laser radiation on superficial and deep sensation, on the electroneurographic parameters of peripheral sensory and motor nerves, on neuropathic pain of the lower extremities in patients with diabetic neuropathy, assessment of side effects and unwanted local or general reactions, comparative analysis compared to placebo-procedures, development of a therapeutic algorithm with MLS-laser.

VII. Material and methods

The study included a sufficient number of patients with EMG-verified diabetic neuropathy - 69, meeting precisely defined criteria. Appropriate measures were analyzed in all: SF-MPQ-2 version of the McGill Pain Objectification Questionnaire, myelinated nerve fiber function by lower extremity vibrosensation with a 128 Hz Rydel-Seiffer tuning fork, touch sensation with 10 gram monofilament of Semmes-Weinstein, of temperature sensitivity with a temperature discriminator, the electroneurographic parameters (distal latency time, action potential amplitude and conduction velocity) of sensory and motor fibers of peripheral nerves of the lower limbs. The cohort comprised an experimental group of 41 patients MLS - laser treated and a matched control group of 28 patients with placebo therapy. Patients were evaluated before the start of treatment, after completion of the therapeutic course (21 days) and on the 90^{th} day from the start of treatment with optimally selected laser parameters and an adequate course of diabetic neuropathy treatment.

The applied research methodology allows to achieve the set goal and to obtain an adequate answers to the tasks to be solved in the dissertation work. Statistical methods have been chosen appropriately for a full and reliable evaluation of the data.

VIII. Main results and contributions of the dissertation work

A large number of results have been obtained and successfully analyzed, which have been systematized and appropriately illustrated with tables, figures and three appendices. The results correspond to the tasks set.

At baseline before therapy, the two study groups were matched in terms of duration of diabetes mellitus and diabetic neuropathy, demographic and anthropometric indicators, as well as in terms of subjective complaints. As a result of the applied MLS-laser therapy, a statistically significant positive effect was achieved in the experimental group, which lasted until the end of the observed period. The reduction of pain, the improvement of superficial and deep sensation, as well as of the electroneurographic indicators for nn. suralis, tibialis and peroneus,

gives Dr. Yosifova reason to recommend deep tissue laser therapy as a monotherapy not only as a non-pharmacological adjunct to standard therapy in patients with painful diabetic peripheral neuropathy.

In the discussion of the dissertation work, Dr. Lili Yosifova compares her own results with those in the modern specialized literature, emphasizing their significance.

In conclusion, the most important results of the study are summarized.

Five clearly formulated conclusions have been synthesized, which accurately reflect the results of the conducted research and fully meet the set goals and objectives.

I accept the scientific-theoretical contributions made by the doctoral student herself - for the first time in our country, an in-depth study of the effect of MLS-laser therapy on diabetic neuropathy is applied and a positive short-term and long-term effects as a monotherapy of diabetic neuropathy are proved. The dissertation student has clearly indicated the contributions of a scientific and practical nature for the positive effect of the new, non-invasive method of treatment with high-power laser radiation and the protocol for its application.

The scientific hypotheses, defined tasks and summaries of the results obtained in the dissertation are original and authentic.

The abstract is structured in accordance with the requirements, and its content fully corresponds to the dissertation work illustrated with 10 tables and 19 figures.

IX. Recommendations

It is appropriate for Dr. Yosifova to publish her studies in some international scientific journals, referenced and indexed in world famous databases of scientific information.

IX. Conclusion

The dissertation work of Dr. Lili Yordanova Yosifova is on a topical topic for our country - "Study of the effect of a high-power laser in diabetic sensorimotor neuropathy", it has been developed thoroughly and comprehensively, it presents scientific, scientific-applied and practical results and conclusions with an original contribution to science and meets all the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB and the Regulations of the University of Varna.

The dissertation shows that the doctoral student Dr. Lili Yordanova Yosifova possesses in-depth theoretical knowledge and professional qualities and skills for independent conduct of scientific research.

All this gives me sufficient reason to confidently give my **positive assessment** of the peer-reviewed dissertation work and to suggest to the respected members of the scientific jury to give their **positive vote** for awarding Dr. Lili Yordanova Yosifova an educational and scientific degree "doctor" in the field of higher education 7. "Healthcare and sport", professional direction 7.1. "Medicine", scientific specialty "Physiotherapy, spa treatment and rehabilitation" at Prof. Dr. Paraskev Stoyanov Medical University - Varna.

10/20/2022

Prepared the review:
Prof. Zlatka Stoineva-Paskaleva, MD, PhD
member of the Scientific Jury