STATEMENT EVALUTAION

by

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On the Dissertation for awarding the educational and scientific degree **"Physical Doctor / PhD"**

Scientific specialty "Dermatology and Venereology"
Doctoral program: "Skin and venereal diseases"
Professional field: 7.1 "Medicine", Field of higher education: 7. Health and Sport

of Dr. Julian Zlatkov Penev,
doctoral student at the "Department of Infectious Diseases, Parasitology, and Dermato-venereology"

entitled **„ Laser Resources for Facial Rejuvenation and Aestheticization"**

Supervisor: Assoc. Prof. Dr. Ilko Bakardzhiev, Ph.D.

General presentation of the procedure

I have been appointed a member of the Scientific Jury under the procedure for public defense of the above dissertation with Order № P-109-152 / 13.04.2022 of the Rector of the Medical University - Varna, pursuant to a decision of a meeting of the Faculty Council at the Faculty of Medicine at MU - Varna under Protocol № 63 / 05.04.2022. The dissertation was approved and directed for Public Defense after hearing a meeting of the Department Council - №14 / 15.03.2022. The documentation presented to me on the procedure is in accordance with the requirements of the Law for development of the academic staff in the Republic of Bulgaria, the Regulations for its application and the Regulations for development of the academic staff of MU - Varna for awarding the educational and scientific degree "Doctor".

I declare that I have no common scientific papers with the author of the dissertation Dr. Julian Zlatkov Penev.

Brief biographical data, career development and qualification of the doctoral student

Dr. Julian Penev was born in 1959 in the Popovo town. After graduating from the 5th high school in Varna in 1977, he completed his regular military service in the ranks of the Bulgarian army from 1977 to 1979. He graduated medicine from the Medical University of Varna in 1986. From 1986 to 1987 works in distribution as a resident radiologist at the District Hospital in Silistra. In 1987 he won a

competition for research associate II degree at the Biotechnical Institute BIOTECH - Varna, where until 1990 he headed the department for the application of lasers for medical and biotechnological purposes. His interest in laser technologies dates back to his student years, when he developed the country's first copper halide laser using its own laser tube design and power supply in the frame of the Technical and Scientific Creativity of Youth (TNTM). As early as 1979, while in the ranks of the Bulgarian National Army, he was awarded a gold medal for the construction of "pulsed nitrogen laser and excitable adjustable dye lasers in the entire visible range" at the National Exhibition for TNTM, Plovdiv. After creating the first stable prototype of this laser system, clinical trials were conducted on a control group of 17 volunteer patients, which were conducted at the Department of Skin and Venereal Diseases (CVD) MU-Varna, led by Prof. Dr. Zlatko Penev, dmn. During his journey at the Biotechnical Institute in Varna, he created in 1988 an industrial laser prototype under the brand name "Triton" and participated in two scientific exhibitions in Plovdiv, 1987 and 1988, where the prototype was approved for clinical testing at Queen Elizabeth Hospital, Adelaide, Australia. According to literature data, these were the first cases of pigmented dermatoses and hemangiomas treated with copper bromide laser in the world. These results were reported in 1984 at the National Conference on Optics and Laser Equipment.

After 1990, Dr. Julian Penev constructed two new improved industrial prototypes of dermatological laser systems based on copper bromide, effectively treating vascular and pigmented dermatoses. He also created an original method for treatment with this laser. The copper bromide laser system was awarded a gold medal at the World Exhibition of the Intellectual Property Organization "EXPO-91".

Since 2000 works in "Outpatient clinic for individual practice for specialized medical care - Prof. Zlatko Penev, MD." In 2004 introduces for the first time in Bulgaria a method for rejuvenation of facial skin with deep ablative resurfacing with CO2 laser. The original author's methodology is registered as a trademark "FasetLift" under number 103448 / 22.10.2018 of the Patent Office of the Republic of Bulgaria.

Dr. Penev is a member of the Bulgarian Dermatological Society, Bulgarian Union of Physicians, and Bulgarian Society of Aesthetic Surgery and Aesthetic Medicine. Fluent in English and Russian.

Relevance of the dissertation topic

The present dissertation focuses on laser therapy of dermatoses located on the head and neck with a carbon dioxide laser. These include dermatoses that are difficult to respond to classical therapeutic methods or leave residual scarring that is unacceptable from an aesthetic point of view - acne, multiple

seborrheic and solar keratoses, hyperpigmentation, hemangiomas, keloids, post-burn scars, facial thraumas and injuries, and signs of aging skin (fine lines, deep wrinkles, elastosis and melasma). The classic methods of managing the above diseases include surgical excision, electrocoagulation, cryodestruction, dermabrasion, thermocoagulation, radiotherapy, all of which aim at destruction that cannot be precisely controlled, so the clinical outcome is variable and depends on the experience of the operator. Plastic facial surgery corrects sagging problems and wrinkles in aging skin, but does not change skin's texture but just tightens it. The outcome of a surgical facelift is highly dependent on subjective factors and the end results are not always predictable and sometimes even grotesque. The same risks apply to hyaluronic fillers, which "fill" the lost volume in the skin, but do not improve its structure.

In recent decades, new lasers and other energy-intensive hardware systems have been actively entering dermatology, but their effects have not been sufficiently clinically studied. The methods for conducting therapeutic procedures with them have not been optimized or specified in clinical protocols. Moreover, the market is encouraging the development of new systems, with a tendency for spontaneity in the emergence of new models without sufficient study of their effectiveness, which fully applies to lasers used in dermatology. The effectiveness of the latter and their therapeutic range are overexposed and create conditions for unrealistic expectations, both in the patient and in the attending physician. Insufficiently detailed models of the biophysical interactions of laser light with the skin have not been developed. All this requires the development of physical models of interaction of laser light with tissues in biophysical aspect, supported by advanced clinical results, characterized by lack of rough scarring and maximum aesthetics of the end result, especially valuable in the face.

The present work is the result of the ambitious and well-achieved goal of the author to summarize his own over 30 years of clinical experience in the treatment of various dermatoses and procedures that improve the appearance and condition of aging skin. The possibilities for application of CO2 laser in the therapy and aesthetization of facial skin are analyzed, comparing and analyzing photo-documentary material from own clinical practice and optimized therapeutic techniques in order to achieve maximum aesthetics of the end result. Based on all this, the topic of the dissertation is extremely relevant and necessary for the Bulgarian dermatological science, both in theoretical and in scientific applied aspect.

General characteristics and structure of dissertation

The dissertation of Dr. Julian Penev is written on 233 standard typewritten pages and includes the usual scientific thesis sections: title page, content, abbreviations - 3 pages; introduction and review of literature - 31 pages; goal, tasks, and hypothesis - 2 pages, materials and methods - 18 pages, results,

and discussion - 129 pages; conclusions - 1 page, conclusion - 3 pages, contributions - 2 pages; bibliography - 6 pages, appendices - 39 pages. The text is richly illustrated with 188 figures - photographs of perfect quality and figures with clear content, 2 graphics, 7 tables, and 6 appendices containing additional photographic material. The bibliography includes a total of 105 sources, of which 20 in Cyrillic and 85 are in Latin.

Review of literature

Review of literature represents the stream of literature data from scientific periodicals related to the application of lasers in medicine, and in particular in dermatology. The beginning of this practice dates back to May 1960, when the first laser shot was fired, and for several decades, the use of laser systems has become increasingly important in medical practice. The overview is logically divided into eight subsections, the first five of which present in understandable and at the same time competent and scientific language the basic physical parameters (energy, power, dose) and characteristics of laser light, the principles of laser beam modulation, guiding, and scanning systems. The text reflects author's profound knowledge of this difficult and quite unfamiliar to the non-specialized audience physical and biological matter and is in itself a modern, interesting, and intelligently written work on laser systems. The review contains sections devoted to the specific interaction of laser light with the skin, and contains a critical analysis of the available literature data on the therapeutic outcome of the application of CO2 laser in various dermatoses. The analysis of laser procedures for rejuvenating facial skin is extremely interesting. An extremely original point of view is proposed that combines evolutionary, phylogenetic, ontogenetic, medico-social, as well as medico-biological approaches in interpreting skin aging process, the involvement of environmental factors (exposome), and skin microbiome involvement. The review convincingly demonstrates that long-term effects of modern physical and chemical interactions with the skin including high-frequency currents, ultrasound, pulsed light, and lasers, are not well studied and motivate the need for this dissertation.

The aim of the dissertation is clearly stated, namely "To optimize, analyze and summarize the therapeutic laser options for aestheticization and rejuvenation of facial skin with specific techniques and typical clinical cases in anatomical areas of the head - kapilitsium, eyelids, ears, lips, nose and neck ”. In relation to it, the dissertation has set 7 tasks, the consistent implementation of which convincingly leads to the goal and the main hypothesis of the dissertation, which convincingly demonstrates that by optimizing the laser action (ablative, thermolysis, and fractionation) non-aesthetic facial formations can be removed to improve the structure and elasticity, and to achieve lasting results that affect positively the self-esteem and quality of life.

Studied material includes a clinical contingent of patients with dermatoses difficult to either respond to classical therapeutic methods (surgical excision, electrocoagulation, cryodestruction, dermabrasion, thermocoagulation, radiotherapy) or scarring is aesthetically unacceptable for the patients -acne, multiple seborrheic keratoses, hemangiomas, keloids, post burns, injuries, and surgery scars, and erase the signs of aging skin (fine lines, deep wrinkles, elastosis, and melasma). The main therapeutic method applied is the treatment of lesions and rejuvenation withCO2 laser, by comparing and analyzing the photographic documentation. The studies were conducted initially in Clinic of dermatology and venereology - Varna and in AISMP "Prof. Dr. Zlatko Penev"(after 1995). CO2 laser destruction was performed using the following techniques: 1) Laser Fast Draw Ablation (LFDA); 2) One-Shot Ablation (OSA); 3) laser excision and incision; 4) laser thermolysis; 5) fractional ablative laser resurfacing. The therapeutic efficacy is compared with that of other known methods. Also included was a control group of 100 patients of both sexes (aged 30-72 years) with dermatoses that violated facial aesthetics, multiple lesions on the head and neck, prolonged adult acne and age-related changes, presenting a neglected and prematurely aged face with severe elastosis and prominent wrinkles. Participants completed twice (before the aesthetic laser procedure and 6 months after it) a psychological questionnaire, which contains 2 self-assessment modules: 1) Appearance related self-esteem through a scale consisting of 11 points (Balabanova, 2018); 2. Multidimensional Self-Esteem Scale / Revised Janis-Field Scale. Appropriate statistical analysis tools (IBM SPSS Statistics, version 20 which allow a confidence level of $p < 0.05$), are selected.

The results of author's own studies and their discussion convince of the merits of scientific development and demonstrate the therapeutic and aesthetic effects of the application of CO2 laser as particularly suitable for removing all benign skin lesions in the head and neck; exceptions are venectasias and decorative tattoos. Laser ablation, thermolysis, and excision are suitable for the removal of unaesthetic dermal melanocyte nevi, papillary nevi, and those that are pediculous. They are suitable for multiple, smaller nevi and solar lentigo, for which surgery is unwarranted or may be associated with gross scarring and keloids. Special attention in presenting the results of laser ablation of seborrheic keratoses, nevi, and vascular dermatoses is paid to some anatomical areas of the head, such as the eyelid, lash line and eyebrows, the area of the nose and near it, lips, and around them, ear and kapilitsium. The therapeutic success is confirmed by the correlation analysis of the application of the scales for self-assessment of appearance and general self-esteem, which are strongly related both before and after aesthetic procedures (respectively $r = 0.62$, $p < 0.01$; $r = 0.49$, $p < 0.01$). The clinical results are supported by photo documentation before and after ablation, and the attached photographs are of enviably high quality.

The dissertation **conclusions** are 4, and although they objectively reflect the tasks and the results of the doctoral student's own research, I believe that based on the rich volume of procedures performed in various dermatoses, their number could be greater. The therapeutic efficacy of the application of ablative CO2 laser effects is supported as a suitable therapeutic alternative, providing high aesthetics of the end result in the removal of pathological lesions on the face. The developed CO2 laser technique is effective in the treatment of prolonged juvenile and adult acne, and fractionated ablative procedures can erase signs of severe acne.

The contributions summarized are 13 in number, 5 scientifically theoretical, and 8 scientifically applied which I accept in full. I accept with admiration the contributions prior to the dissertation presented in Appendix 1, although they could be a subject of a separate author's monograph.

The abstract adequately reflects the main points of the scientific development and makes an impression that it contains quality photo documentation of the results achieved.

Publications related to the dissertation

A sufficient number of publications have been presented in relation to the topic of the dissertation - a total of 8 articles in English in international peer-reviewed publications, of which Dr. Penev is the lead author. Related to the dissertation are 4 monographic works, as well as 14 participations in scientific forums, are included.

Critical remarks

I have no remarks on the essence of the dissertation. Some technical remarks, such as a few grammatical and spelling mistakes can be mentioned: e.g. page 26 - xanthelasma; in some cases dermatological diagnoses are cited in both Latin and Bulgarian, while it would be good to unify them. The use of some foreign terms is kept to a minimum and has it's explanation in the vast amount of information and English terminology that has entered medical practice in recent years, especially in the highly specialized field of lasers. Some abbreviations used, although well known and established, are subject to introduction after their widespread use, e.g. Sun Protecting Factor / SPF.

I believe that these remarks do not harm in any way the scientific value of Dr. Penev's dissertation.

Conclusion

I believe that the dissertation of Dr. Julian Zlatkov Penev, entitled " Laser Resources for Facial Rejuvenation and Aestheticization" is originally conceived and developed with the correct definition of

purpose and objectives, with the right selection of clinical material and applied methods, with richly illustrated, critically analyzed and convincingly presented results. The work is fully in line with modern trends in efficiency, yet also aesthetically acceptable for various dermatoses on the face. Against the background of the desire to avoid unaesthetic and scarring changes from "classical" destruction methods' results, the dissertation demonstrates the author's master-made, as well as scientifically based technique based on the selection of appropriate laser parameters, which leads to lasting efficiency and improvement of psycho-emotional self-esteem of patients.

This gives me a reason to recommend to the esteemed members of the scientific jury to give their positive vote and to judge Dr. Julian Zlatkov Penev's educational and scientific degree "Doctor".

Sofia, May 2nd, 2022

Reviewer:

(Prof. Snejina Vassileva, MD, PhD)