

To the Scientific Jury  
Constituted by the Rector  
of MU "Prof. Dr. Paraskev Stoyanov" Varna  
By order № P-109-211 / 28.04.2021

OPINION

From Assoc. Prof. Dr. Teodora Nedeva, MD, PhD

RU "Angel Kanchev", FOPHHC, Department of "Medical, clinical and diagnostic activities", Deputy  
Head;

COC- Ruse, Department of AICU- doctor

Subject: Dissertation on "Ultrasound examination of the optic nerve in patients with clinical and  
imaging evidence of increased intracranial pressure",

in the scientific specialty "Anesthesiology and Intensive Care", professional field 7.1 Medicine.

Author of the doctoral thesis: Dr. Nikolai Valentinov Mladenov

**Dear Colleagues,**

I received a set of documents which contained: orders, declarations, CV, abstract of doctoral thesis, list of publications and dissertation of Dr. Nikolay Valentinov Mladenov. Their type and volume completely fulfill the requirements for the development of the academic staff in MU Varna, for awarding ESD "Doctor". According to the order of the Rector of MU "Prof. Dr. Paraskev Stoyanov" Varna, with № P-109-211 / 28.04.2021, I am included in the Scientific Jury. After a decision from its first meeting, I am appointed to prepare an opinion on the dissertation (report № 1 / 28.04.2021 ).

- 1. Brief biography of the researcher:** Dr. Nikolay Mladenov was born in 1988 in Varna, where he completed his primary, secondary and higher education. Since 2013, he has been working in the Department of AIC at the University General Hospital for Active Treatment "St. Marina" Varna. Since 2015 he has been an assistant at MU Varna. In 2018 he acquired the specialty "Anesthesiology and Intensive Care". He is a coordinator of donations and transplantation of the hostital he works in. He teaches Bulgarian and foreign students in the fields of Anesthesiology and Intensive Care and Emergency Medicine. Regularly participates in international projects. He is a member of the Society of Anesthesiologists in Bulgaria. He has 10 publications in Bulgarian and foreign bulletines.
- 2. Annotation of the problem:** Intracranial pressure (ICP) is a complex disorder. Its increase is a life-threatening condition that triggers a cascade of pathological processes and vicious circles. Often the symptoms of intracranial hypertension (ICH) are not strictly specific and sensitive

and appear only when high values of ICP are reached. Remaining unrecognized or inadequately treated, they severely or irreversibly damage brain structures. The treatment of critically ill patients with CNS pathology requires from the intensive care physicians knowledge of the genesis of increased intracranial pressure, adequate treatment and monitoring. Various methods of invasive and non-invasive assessment and follow-up of High ICP are known. Transbulbar ultrasound to assess the diameter of the optic nerve is a non-invasive innovative method for Bulgaria, which is accessible and easy to assimilate. It can be very useful in the detection, monitoring and treatment of intracranial hypertension. Moreover, in the last decade there are not many Bulgarian authors to study this technique or to offer scientific publications related to its application in our everyday practice. This definitely makes the subject of Dr. Mladenov's scientific work very innovative, interesting and definitely dissertable.

- 3. Analysis and evaluation of the dissertation:** I approach the work of my colleague with the clear awareness that dissertations are usually unique works, without strictly fixed frameworks, but they follow exemplary models established over time by the scientific community.

**3.1. General volume and structure:** The present dissertation contains a total of 112 standard pages. The author's research and literature data are presented to the readers in 10 sections, the second and fourth of them having subsections. It is illustrated with 5 tables and 32 figures. The distribution of information is as follows: Abbreviations used in the text - 1 page, Introduction - 1 page, Literature review - 32 pages, Goal and objectives of the dissertation project - 1 page, Clinical study objects and methods - 14 pages, Results - 30 pages, Discussion - 6 pages, Conclusions - 1 page, Contributions - 1 page, Bibliography - 12 pages, and List of publications on the topic - 1 page.

**3.2. Format and content of the sections:** My assessment is that the work is written clearly, concisely and in an understandable manner, with very good expression and style. The "Content" section lists the pages of the various sections, which allows us to find them quickly and easily in the presentation. The layout and formatting of the pages is good and thus ensures easy reading of the information. All tables and figures have clearly formulated explanations, which facilitates the understanding of the obtained results. The different sections of the thesis are titled according to the generally accepted models.

*Section "Introduction":* presents the main characteristics of the researched problem and the position of the author regarding his choice to study this particular topic. What is valuable for me is the fact that the dissertation has also presented historical aspects of the nature of ICP.

*Section "Literature review":* the definition of ICP and its normal reference values are presented. The nature and pathophysiological features and connections of ICP with the other intracranial components are described in details. Studies and positions of various foreign authors about possible diagnostic methods and techniques for diagnosis and monitoring of ICP are discussed. Special emphasis is placed on the concept of ultrasound examination of the optic nerve. In great details are presented the historical development of ultrasound diagnostics and its application in intensive care medicine. Theoretical and illustrational introduction of the anatomical features of the optic nerve and the influence of the increasing intracranial pressure on its shells and its diameter are made. Ultrasound models are described precisely and it is well explained that they can be used either to assess normal structures and various pathological conditions leading to HICP or for monitoring this parameter in dynamics. Various comparative studies of authors using ultrasound for the diagnosis of HICP have been mentioned and the results of CT, MRI and some invasive techniques have been compared. Respectively, advantages and disadvantages of each technique are discussed. A special place is granted to the concept of "Brain Death" and the possibility of the HICP in potential organ donors to be examined with ultrasound. In my opinion this is a very reasonable focus and an appropriate study for a coordinator of donation and transplantation. I am very impressed by the summarized analysis of the literature data, which naturally and logically followed the main goal and tasks that the author of the thesis sets at the beginning of his research. It is accepted that the literature review is about 30% of the total volume of work. In the current one, this is not fully observed.



*Goal and objectives of the dissertation project:* developed as required. The main purpose of the study and the six tasks related to it are formulated clearly and concisely and I fully accept them in this form. *Section "Clinical study object and methods":* The work was developed on the basis of 2 years of prospective study, without specifying exact dates. 86 patients over 18 years of age with suspected or proven CNS pathology leading to ICP were included. They were compared with a control group of 52 healthy volunteers. Criteria for inclusion and exclusion in the study are clearly formulated. It is approved by the Ethical Committee of MU Varna and patients are included after signing an informed consent personally or by a family member. Verbal explanation for the nature of the study was provided. The patients in the experimental group were divided into 4 subgroups, with a different number in each of them. The subgroups differ not only in the number of patients, but also in the type of CNS pathology, gender, body weight and age.

The distribution of patients in each specific subgroup and the stratification by different criteria - gender, age, diagnosis, body weight assessment by ASA are defined in details.

*The "Methodology of the clinical study"* describes the methods of assessment and follow-up of the patients involved - history, clinical examination, laboratory tests, imaging techniques. A good illustrative and verbal presentation of the used ultrasound machine, the techniques of localization of the optic nerve and measurement of ONSD, in sagittal and transverse position, the frequency and rhythm of ultrasound examinations are represented. The principles for diagnosis and evaluation of IICP with CT of the brain and the interpretation of the results obtained by imaging specialists are described. The technique of four-vessel cerebral angiography for the assessment of cerebral blood flow in BD is also well presented. The treatment methods - craniotomy, mechanical ventilation, diuretic therapy are described in subsections and give the reader a good idea of their administration. I appreciate the fact that the researcher himself conducted all ultrasound examinations.

The data is analyzed with up-to-date software products, including classic and newer data analysis. They are consulted by a specialist in medical statistics, which greatly minimizes the possibility of errors in obtaining reliable results.

**5. "Results" section:** in detail, on 29 pages, the data from the scientific research is presented in tabular, graphical and narrative form.

**6. "Discussion" section:** compare the author's results with those published in world literature. The solution of the tasks set and the fulfillment of the main goal of the research are presented. I believe that the results obtained are valuable for our daily practice in ICU. It would be appropriate for the researcher to present them to a wider audience as they can be useful for the anesthesiology community in our country.

**7. "Conclusions" section:** 7 conclusions are clearly and concisely formulated. I accept them without any remarks.

**8. "Contributions" section:** the division of contributions into 2 groups is a customary practice. All 6 of them are described in an understandable way and I accept them all.

The author also presents all the applications and forms he used for his research.

**"References" section:** 178 sources are cited, which are sufficient for a detailed study of the experience of different researchers. They are arranged in alphabetical order, starting with those in Cyrillic, which is essentially correct. There are only 7 Bulgarian publications. This confirms the uniqueness and dissertability of the investigated method. Regarding the period of publication of the literature used - the main proportion is borrowed by publications printed before 2010. Only 70 of the titles have been printed in the last decade.

The author presents 4 scientific publications, 3 of which concern the topic of the dissertation. According to the requirements of MU Varna, this is a sufficient publishing activity for the acquisition of ESD "Doctor".


**Abstract:** According to some scholars, it is considered an independent publishing activity. According to others, it is an integral part of the dissertation and should be analyzed together with it. The information in the abstract is presented on 59 pages. In a compressed version, the readers are offered the content of the dissertation. In my opinion, this is appropriate because it allows the reader to get

acquainted with the basic thesis of the scientific research along with quick and easy introduction to the results and conclusions.

***Conclusion: related to the aforementioned, I think that the presented dissertation is very valuable in practical and scientific terms.***

***I am thus certain in granting POSITIVE assessment of the scientific thesis and vote "YES", to award the ESD "Doctor" to Dr. Nikolay Valentinov Mladenov***

12.05.2021

Prepared the opinion: .....

/ Assoc. Prof. Teodora Nedeva, MD ,PhD/