

**TO THE CHAIRMAN OF THE SCIENTIFIC JURY  
DESIGNATED BY A WRITTEN ORDER Nr. P-109-211/28.04.2021  
OF THE RECTOR OF MEDICAL UNIVERSITY OF VARNA**

**STATEMENT OF OPINION**

**By Assoc. Prof. Georgi Angelov Pavlov, MD, PhD  
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On doctoral thesis "**Ultrasound examination of the optic nerve in patients with clinical and imaging evidence of increased intracranial pressure**" for awarding educational and scientific degree "Doctor of Philosophy" in doctoral program in Anesthesiology and Intensive Care.

**Doctoral candidate:** Nikolay Valentinov Mladenov, MD- Assistant Professor, Department of Anesthesiology, Emergency and Intensive Care Medicine, Medical Faculty, Medical University of Varna

**Scientific Supervisor:** Prof. Vilian Hristov Platikanov, MD, PhD- Head of Department of Anesthesiology, Emergency and Intensive Care Medicine

**1. General presentation of the procedure and the doctoral student.**

The presented set of documents and materials is in accordance with the Inner Regulations of Medical University of Varna and Art. 69 of the Regulations for the Development of the Academic Staff of Medical University of Varna.

Nikolay Valentinov Mladenov, MD was born in 1988 in the city of Varna. He graduated his Master's degree in Medicine from the Medical University of Varna in 2013. In the same year he started his medical practice as an anesthesiologist intensivists in the Department of Anesthesiology and Intensive Care at the University Hospital "St. Marina" in Varna where he is still working so far. In 2018 after successfully passing the state exam Nikolay Mladenov, MD was recognized as a specialist in Anesthesiology and Intensive Care. From 2015 until now he has been working as an assistant professor in the Department of Anesthesiology, Emergency and Intensive Care Medicine at Medical Faculty of Medical University of Varna. The candidate is fluent in English.

**2. Relevance of the topic**

Critical illness from severe central nervous system (CNS) injury is a common pathology in intensive care units involving in a significant proportion of cases young people in active creative ages. Despite significant advances in intensive care in recent years, these conditions are still associated with unacceptably high mortality rate and permanent disability especially in cases with late diagnosis and inadequate treatment which makes them a problem with enormous medical, economic and social impact. Not only do the extremely diverse and numerous etiological factors cause direct deleterious effects on the CNS structures, but they also cause indirect damage by increasing intracranial pressure and compromising in that way the adequate cerebral perfusion and oxygenation. The syndrome of intracranial hypertension is the most significant universal pathogenetic mechanism in the development of critical illness associated with severe CNS injury. It determines to the greatest extent the disease course, prognosis and outcome which makes monitoring of intracranial pressure a vital component in the diagnosis and treatment of this patients' group. Although invasive techniques for measuring and monitoring intracranial pressure are considered the "gold standard", there are a number of risks and complications related to their use. That is why alternative methods for early

diagnosis of intracranial hypertension, monitoring its dynamics and assessing the effect of treatment have recently been searched.

Ultrasound assessment of optic nerve diameter is a relatively novel, non-invasive and original intracranial pressure monitoring method which enables early recognition of intracranial hypertension. It is fast, beam load free, easy to perform by the bedside, with the possibility for repeated recurrence and does not require continuous staff training. Besides, the lack of complications and drawbacks of the invasive monitoring techniques makes the ultrasound measurement of optic nerve diameter an attractive and useful method in intensive care medicine. That is why I strongly believe that the topic of the doctoral thesis of doctoral student Nikolay Mladenov, MD is an exceptionally relevant, contemporary and promising problem of great practical importance which has not been the subject of scientific research in Bulgaria yet.

### **3. Characteristics and evaluation of the doctoral thesis**

The thesis represents a completed scientific work. It is properly constructed and includes all the relevant sections following the established specific form. It is written in an understandable grammatically correct Bulgarian in accordance with the scientific nature of the paper. The following sections are included in the thesis: Introduction - 2 pages; Literature Review - 35 pages; Aim and Tasks - 1 page; Object and Research Methodology - 15 pages; Results - 30 pages; Discussion - 6 pages; Conclusions - 1 page; Contributions - 1 page; Appendices - 7 pages and Bibliography - 12 pages. The doctoral thesis is written on a total of 112 pages. It is well illustrated with 32 figures and 5 tables.

**The bibliographic reference** covers 178 titles of which 7 in Cyrillic and 171 in Latin. It is in accordance with the citations in the PhD thesis.

**The title** is clearly formulated and sufficiently informative. It reflects adequately the content of the research and corresponds to the presented data and conclusions.

**The literature review** is a systematic and comprehensive presentation of the research subject. It highlights the controversial and unsolved issues in worldwide and national clinical practice. It is written in short and comprehensible sentences which makes it easy and pleasant to read. The review gives enough information about increased intracranial pressure in various pathological conditions considering the various methods for its monitoring and their clinical significance. Ultrasound evaluation of the optic nerve is very well presented as a modern possibility for evaluation of the intracranial pressure with its advantages and disadvantages. The presented literature review allows the author to analyze various aspects of the problem as well as to determine the main goal and the priorities of the scientific research.

**The main goal** of the doctoral thesis is correctly defined and clearly and precisely formulated. It is in unison with the title of the thesis and corresponds to the further development of the scientific research.

**Tasks** – the candidate has set 6 tasks aimed at fulfilling the main goal. They are formulated accurately and academically describing the actions needed to be done. However, I believe that their number could be reduced to 3 or 4 by merging some of them.

**The section "Object and Research Methodology"** represents the subject, the object and the design of the study accurately. It is very well structured and properly presented. The different groups of patients are very well described as well as the overall methodology of the research. The research materials and methods are correctly and precisely selected to fulfill the main goal and tasks. The inclusion and exclusion criteria are carefully formulated making it possible to minimize all the factors that could affect the accuracy and reliability of the results. The technique of conducting the research and technical characteristics of the equipment used are presented in great detail and systematically. A wide range of modern and accurate statistical tests has been used for statistical processing which guarantees the reliability of the obtained results and the conclusions made.

**The obtained results** correspond to the set tasks. Their description is supported by detailed graphic and tabular material with comprehensive text descriptions. On the basis of the obtained results it has become clear that the ultrasound examination of the optic nerve is a relevant method for objective assessment of changes in intracranial pressure and the effect of treatment.

**Discussion-** in this section Nikolay Mladenov, MD analyzes and discusses the obtained results making in some places comparisons with data from the literature used. However, the author's critical and creative conclusions prevail.

**Conclusions-** the essential part of the PhD thesis ends with the formulation of seven conclusions that I completely agree with. They are all well presented and structured corresponding to the main goal and tasks of the thesis.

**Contributions** – the PhD candidate proposes 6 contributions divided into two groups - scientific-practical and scientific-theoretical. I accept the contributions without remarks.

#### **4. Abstract**

The abstract is prepared in accordance with the requirements of the Regulations of MU-Varna. It is written on 60 pages. The abstract summarizes well the structure of the doctoral thesis and contains the most important studies, results, conclusions and contributions. It is illustrated with a sufficient number of figures and tables.

#### **5. Assessment of the publications and personal contribution.**

Nikolay Mladenov, MD has presented four publications in reference to the PhD thesis. He is the first author in two of them, and the second author in the others. The articles have been published in a peer-reviewed scientific journal, refereed and indexed in the world – renowned scientific information databasis Scopus. However, I consider that the 2nd and 4th publications on the list presented are not relevant to the research.

#### **6. Critical remarks and recommendations:**

6.1. I could point out as a critical note that the author should have compared the ultrasound examination of the optic nerve with the invasive intracranial pressure monitoring techniques, established as a "gold standard", in order to investigate its clinical significance and value as a method of assessment, follow-up and prognosis in critically ill patients with severe brain injury and intracranial hypertension.

6.2. I believe that it would be invaluable for the whole work if a group of patients with severe traumatic brain injury were included so that the importance of ultrasound in the assessment of the disease severity, treatment effect and prognosis among this significant population in ICU to be studied.

6.3. I think that the doctoral candidate should promote the results of his research by preparing and publishing scientific articles in peer-reviewed scientific journals refereed and indexed in world – renowned scientific information databases (Scopus & Web of Science), including those with an Impact Factor.

#### **CONCLUSION**

Despite the critical remarks, I strongly believe that the doctoral thesis "Ultrasound examination of the optic nerve in patients with clinical and imaging evidence of increased intracranial pressure" by Nikolay Valentinov Mladenov, MD meets all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria, The Regulations for its application and the Inner Regulations of Medical University of Varna. This is the first study in Bulgaria with generalized observations and conclusions on the application of ultrasound examination of the optic nerve in

patients with intracranial hypertension. It is an independent contemporary study with significant scientific results which shows that the PhD Candidate Nikolay Valentinov Mladenov, MD has in-depth theoretical knowledge and professional skills in the specialty of Anesthesiology and Intensive Care demonstrating qualities and skills for independent scientific research.

Taking into account all the abovemention facts, I grant my positive assessment of the study presented by the reviewed doctoral thesis, abstract, results and contributions by proposing to the members of the honorable Scientific Jury to give their positive vote for awarding the educational and scientific degree "Doctor of Philosophy" to Nikolay Valentinov Mladenov, MD in doctoral program in Anesthesiology and Intensive Care.

17.05.2021



Assoc. Prof. Georgi Pavlov, MD, PhD