REVIEW

by

Prof. Yavor Enchev, MD, PhD
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on the doctoral thesis on the topic of:
"Multimodal electrophysiological neuromonitoring in neurosurgical operative interventions"

for the award of the educational and scientific degree "Doctor"
in scientific specialty Neurosurgery, code 03.01.41
in professional field 7.1. Medicine, 7. Health and sports.

Author of dissertation: D-r Milko Dimitrov Milev,
Neurosurgeon at the Neurosurgery Clinic
in Acibadem City Clinic University Hospital Tokuda

Scientific supervisor: Assoc. Prof. D-r Vladimir Stefanov Nakov, MD, PhD

General remarks and comments to the procedure:

By Order No 15-03-393#1 from 18.11.2022 of the Executive Director and the Procurator of Acibadem City Clinic University Hospital Tokuda, I was appointed as an external member of the Scientific Jury in relation to the dissertation of D-r Milko Milev and to present an Opinion. The defence procedure fully meets the requirements of the current regulatory framework in the Republic of Bulgaria – the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of the Law, as well as the Regulations on the Development of the Academic Staff at Acibadem City Clinic University Hospital Tokuda.

D-r Milko Dimitrov Milev was enrolled in doctoral studies by Order No 292 from 26.07.2019 of the Executive Director and the Procurator of Acibadem City Clinic University Hospital Tokuda. He has completed the individual doctoral plan and has successfully passed the required exam from the individual plan for doctoral studies. On 25.07.2022, the completed dissertation was presented to the Extended internal Scientific Jury, after which, by Order No 15-05-137 from 30.09.2022 D-r Milev was deducted with a right of defence.

The dissertation, its abstract and the required documents and materials related to the official defence procedure provided by the doctoral student fully meet the legal requirements of the afore-mentioned regulatory framework.

Short biographical data:

D-r Milko Dimitrov Milev graduated in "Medicine" in 2010 from the Medical University of Sofia. In the period 2011-2016 he specialized in the Clinic of Neurosurgery of UMHATEM "N. I. Pirogov" and in the Clinic of Neurosurgery of "Acibadem City Clinic UMHAT Tokuda", acquiring the specialty of "Neurosurgery" after passing a state exam in 2016. D-r Milev has undertaken additional courses and trainings in the field of the doctoral thesis thematic – Research Course of the European Association of Neurosurgical Societies (2011), three-year cycle of the Educational Course of the International Society of Intraoperative Neurophysiology (2018-2021), IRCAD Masterclass – 360-Degree Skull Base Surgery (2021).

Relevance of the problem:

The doctoral thesis expands on the subject of electrophysiological monitoring in intracranial neurosurgical interventions, discussing in particular the need for multifactorial analysis of the clinical characteristics of the patient, the nature and course of the surgical intervention and the observed electrophysiological phenomena for the accurate and prompt determination of risk points and actions related to increase in the risk of neurological damage. The available literature information is limited in the scope of its analysis and addresses the problem one-sidedly, it is based on relatively limited clinical series and does not take into account the complexity of phenomena and events in neurosurgical operative practice, thus giving an impression of a lack of congruence in the practical guidelines and the conclusions of the earlier studies. The aforementioned facts define the topic of the dissertation as relevant and socially significant.

Structure and characteristics of the dissertation:

The literature review examines over 23 pages the characteristics of intraoperative monitoring of motor cortex and cortico-spinal pathways and of oculomotor nerves, the different criteria for elucidation of the location and functional state of these motor systems. Problematic aspects in the determination of the risk of neurological damage have been identified as well as the potential for the application of different electrophysiological criteria for this purpose. The need to conduct multifactorial analysis in the exploration of the interrelations between different predictive factors, in the identification of informative threshold values of electrophysiological criteria and for the achievement of higher level of dependability of the latter is demonstrated. The analysis was conducted in its main part on published scientific material from the last two decades, while at the same time referring to publications of historical, fundamental and cornerstone significance.

The scope and content of the chapter show that the doctoral student is thoroughly familiar with the aspects of the topic, the conclusions from the literature review give a reasonable argument for undertaking the following own research.

The aim of the dissertation, to establish a complex of electrophysiological criteria in order to ensure prompt and reliable identification of an increased risk of damage to motor cortex and cortico-spinal pathways and to oculomotor nerves, is clearly formulated, justified by the analysis of the available literature. Six tasks for each of the two clinical subgroups have been formulated; they are specific, clear and approachable.

Material and methods: The dissertation is based on the analysis of 174 operative clinical cases, divided into two clinical subgroups – cases with mapping and monitoring of the primary motor cortex and cortico-spinal tract (130 cases) and of the oculomotor nerves (44 cases and 61 monitored nerves). The volume and the quality of the material are sufficient to achieve the tasks of the dissertation. The methods for data processing and analysis of the results are reliable, dependable, modern and innovative.

Original protocols for positioning of intraorbital electrodes for oculomotor nerve monitoring under ultrasound control are presented. Specific graphical methods for analysis of the predictions of machine models in conjunction with the observed postoperative results are also proposed.

Results and discussion: The results of the study in both clinical groups are presented in detail (on 80 pages, descriptively and graphically) and are precisely analysed (in 24 pages). The results are sufficient in their volume, correspond to the set tasks and allow statistical processing and analysis to be conducted. A step-by-step analysis of the different electrophysiological criteria for increased risk of neurological damage, as well as the factors modifying the risk of neurological damage and of the analysed electrophysiological criteria is performed. Predictive classification models were generated, ready for application in practice and with defined critical values of the range of factors associated with a significant increase in the risk of damage to the studied functional system. The values of percentage change of amplitudes of direct cortical and transcranial motor evoked potentials associated with an increased risk of postoperative motor deficiency of varying degrees in operations on supratentorial tumours are established. Minimum values of intensity of subcortical stimulation with resulting motor response, which are associated with an increase in the aforementioned risk are also identified, as well as the combinations of conditions permitting the realisation of the potential deficit. A subgroup of operative cases at higher risk for oculomotor deficit are found, criteria for negative prognosis in terms of postoperative deficit of n. abducens are given. Guidelines for the implementation of dynamic graphical analysis of intraoperative electrophysiological findings in the context of the risk of postoperative motor deficit are proposed, that allow for prompt and reliable acquisition of information about the latter, as well as permit the analysis of the complex interactions between two or more dynamically changing electrophysiological indicators.

Conclusions and contributions:

The results of the study and their analysis in the context of previously published studies logically and readily lead to 5 conclusions in the field of motor cortex and cortico-spinal tract monitoring and 7 – in that of monitoring of oculomotor nerves.

The dissertation proposes 2 theoretical, 4 methodological and 4 practical contributions. I accept all proposed contributions.

Evaluation of the publications and the personal contribution of the doctoral student.

D-r Milev presents 6 full-text scientific publications – 5 in Bulgarian and 1 in foreign scientific periodicals, on the topic of the dissertation, as well as five papers presented at scientific conferences and congresses.

Abstract:

The dissertation abstract meets the requirements in terms of volume and content, is built in a way that presents in a sufficiently straightforward way the essence of the scientific work and reflects in sufficient detail the results attained and the conclusions reached.

Conclusion:

The doctoral thesis "Multimodal electrophysiological neuromonitoring in neurosurgical operative interventions" by D-r Milko Dimitrov Milev presents significant results and has valuable theoretical, methodological, and practical contributions that represent an original contribution to science. It meets all the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for the Implementation of the Law and the Regulations on the Development of the Academic Staff at Acibadem City Clinic UMHAT Tokuda. The presented materials and results of the study fully comply with the specific requirements, are original in their nature and no plagiarism has been proven.

The dissertation works show that D-r Milev holds in-depth theoretical knowledge and professional abilities in the field of the researched topic and shows qualities and skills needed for independent scientific research. The attained results, the conducted analysis, the conclusions and the contributions of the work prove the personal merits of the doctoral student.

Due to the above, I give my positive evaluation for the doctoral thesis on the topic of "Multimodal electrophysiological neuromonitoring in neurosurgical operative interventions" and I propose to the members of the venerable Scientific jury to award the educational and scientific degree "Doctor" in the doctoral program of "Neurosurgery" to D-r Milko Dimitrov Milev.

16.12.2022
Varna

Sincerely:
Prof. Dr. Yavor Enchev