From Prof. Dr. Hristo Tsekov Tsekov, MD, PHD, Head of the Clinic of Neurosurgery Of Acibadem City Clinic, Tokuda Hospital, EAD - Sofia

Subject: Dissertation paper "Neuronavigated needle biopsy in cranial neurosurgery" presented by Dr. Martin Nikolaev Moynov, assistant at MU "Prof. Dr. Paraskev Stoyanov "EAD, Varna; UMHAT "St. Marina" EAD, Varna - Clinic of Neurosurgery for the acquisition of educational and scientific degree "Doctor" in the scientific specialty "Neurosurgery".

Dr. Martin N. Moynov was born in Veliko Tarnovo in 1985, and in 2004 he completed his secondary education at the Fourth Language High School "Frederic Joliot Curie" in Varna. In 2012 he graduated with a Master's degree at the Medical University of Varna. He followed a specialization in neurosurgery at the Clinic of Neurosurgery at the Medical University of Plovdiv, and then continued the specialization at the University Hospital "St. Marina" at the Medical University of Varna. In 2017 he was accepted as an assistant at the Clinic of Neurosurgery at the Medical University of Varna, and the following year he was enrolled as a doctoral student at the same clinic studying "Neuronavigated needle biopsy in cranial neurosurgery" with Dr. Yavor Enchev as his supervisor.

In 2019 he was recognized as a specialist in neurosurgery.

As a student and young doctor he has received numerous certificates for valuable clinical research, for participation at home and abroad in scientific conferences and congresses. He has conducted many specializations at home and abroad / France, Ghana, Palestine, Romania, Switzerland /. He is a member of Bulgarian Neurosurgery Society, he is also a member of the international AO Spine society since 2017.

All administrative requirements by the Academic Development Act in the Republic of Bulgaria have been met.

In connection with the dissertation, two full-text articles / 2018 and 2022 / and two papers presented at conferences in Bulgaria and Colombia / 2019 and 2022 / were presented.

An abstract is also presented - 80 pages, designed according to the requirements.

The dissertation itself has a volume of 173 standard typewritten pages. The structure is: Introduction - 1 page, Literary review - 34 pages with formulated Objectives and tasks - 1 page, Materials and methods - 36 pages, Results - 57 pages, Discussion - 25 pages, Conclusions and Contributions - 1 page each. The material is richly illustrated with 135 figures and 70 tables.

The author's idea is interesting and relates to the search for a solution to one of the main problems in neurosurgery and in particular in neurooncology - obtaining material for histological assessment by an easy and relatively low risk method. It is interesting to know that the cause of death in the Republic of Bulgaria in men is 3.7% and 4% in women from primary brain tumors. Brain metastases, in turn, affect 30% of all patients with extracranial tumors. These data strongly confirm the relevance of the problem related to the provision of rapid, low-risk and reliable histological

diagnosis, which is a determining factor for the timely application of non-surgical treatments. Of course, in neurooncology surgery undoubtedly remains the main method of treatment, but in a significant number of cases it is inapplicable (seriously ill, side effects, insurmountable religious barriers) or the intervention itself is too risky / tumors of the basal ganglia or tumors localized in functional active and vital areas. It is in these patients that the application of relatively less aggressive techniques and risk techniques has its significance. Moreover, the conduct of radiotherapy and chemotherapy "blindly" - without histological analysis, leads in 25% to unsuccessfully planned treatment, due to the discrepancy between the diagnosis based only on imaging studies and the final diagnosis. Such a method of diagnosis is the neuronavigated needle biopsy, the efficiency and applicability of which the author aims to prove in the presented work. The dissertation makes the theoretical development in the literature review, which covers 260 current and related titles. It is interesting that all titles are in Latin and none in Cyrillic, which does not mean that there are no publications in Bulgarian literature. There is also serious research, incl. dissertation on this problem - things that deserve more attention, science knowledge in general usually evolves and do not arise spontaneously from nothing. The advantages of minimally invasive surgery in combination with neuronavigation stand out from the literature review. The author correctly considers the deficit in the world literature of adequate assessment of the efficiency and accuracy of frameless surgical equipment, the lack of standards for its application, which makes it difficult to perform an objective analysis of operational results obtained in different surgical techniques and various studies.

From the analysis of the literature review quite logically derive the goal and the tasks necessary for its achievement, namely:

Objective: Analysis and summary of the experience gained with neuronavigated needle biopsy in patients with supratentorial intraaxial lesions, in order to optimize the application of minimally invasive neuronavigated technique for diagnosis and treatment. Based on the obtained results to formulate and introduce a surgical algorithm for the application of neuronavigated needle biopsy and evaluate the effect of its application in the routine practice of the Neurosurgery clinic of University Hospital "St. Marina", Varna.

Tasks:

- 1. To follow and to summarize the results of neuronavigated needle biopsy interventions in patients with supratentorially located intraparenchymal lesions.
 - 2. To make a critical comparative analysis of one's own results with those of other authors.
- 3. On the basis of a thorough literature review of the existing specialized literature to formulate indications for the use of neuronavigated needle biopsy in patients with supratentorial intracranial lesions.
- 4. To analyze the complications and technical difficulties of the neuronavigated frameless surgical technique and to identify guidelines for their reduction.
 - 5. To assess the effectiveness of the procedure and the risks associated with it.
 - 6. Develop a neuronavigated needle biopsy protocol.
- 7. To carry out training of the medical neurosurgical team of the Clinic of Neurosurgery of the University Hospital "St. Marina "on the nature, objectives and use of a neuronavigated needle biopsy protocol in patients with intracranial lesions.

The subject of the analyzes were 40 patients treated for the period January 2019-December 2021, in 15 cases only isolated supratentorial intraaxial lesions were performed, and in the remaining 25 after the biopsy neurosurgical treatment was performed. For all interventions in the study, a planning system / Medtronic @ Planning Stealthstation S7 / was used, located outside

the operating room and allowing calm discussion of the results of imaging studies and proper planning of the upcoming diagnostic and therapeutic procedures.

The modern neurovigation system / Medtronic @ Stealthstation S7 / with infrared camera and reference frame with passive spheres for neuronavigation, as well as adapted tools, which is a guarantee for the quality of the conducted examinations and manipulations, is used for the biopsy. A program for staff training for the safe and effective implementation of the entire procedure has been developed.

Modern methods for statistical analysis are applied: descriptive and analytical analysis, and the obtained data are processed statistically with computer program SPSS v 23, Jamovi 2.2.0 and Microsoft Excel, Winoows 10.

The results included biopsy of 40 patients with 41 supratentorial lesions from a preoperative diagnosis of a total of 50 lesions. The collection of the biopsy material was performed with one punctured trepanation hole and one biopsy trajectory, and in 95% of the cases the obtained material is sufficient for the examination, ie. these are successful biopsies. According to literature data, this percentage is 73% -100%, which is a good attestation for the author and the team conducting the research.

In two of the patients (5%) the biopsy was declared unsuccessful, but in my opinion this is simply a discrepancy between the preoperative and the final diagnosis. No permanent complications were reported, all patients were referred for the next stage of treatment - radio- and chemotherapy, as well as for subsequent radical excision of the tumor.

The discussion is detailed, it analyzes in parallel the data from the literature analysis and own results, which is extremely informative and critical.

A Modified Universal Neurosurgical Checklist has been created, which creates security in the work of the team performing this type of interventions, and is a prerequisite for later comparative analyzes on a larger scale. As a final result, it was reported that frameless neuronavigated biopsy can provide reliable histology in up to 100% of biopsied patients, based on which reasonable planning of further behavior is performed - radical excision, radio or chemotherapy, and combining them. Complications are up to ten percent, but no cases of fatal outcome or severe morbidity have been reported.

The author also forms his contributions:

- 1. Introduction of a surgical protocol for the use of neuronavigated needle biopsy and evaluation of the effect of its application in the routine practice of the Clinic of Neurosurgery at the University Hospital "St. Marina", Varna.
- 2. Implementation of training of the medical neurosurgical team of the Clinic of Neurosurgery at the University Hospital "St. Marina", on the nature, objectives and use of the Navigational Needle Biopsy Protocol in patients with supratentorial intracranial lesions.
- 3. On the basis of a thorough literature review of the existing specialized literature, indications and contraindications for the use of neuronavigated needle biopsy in patients with intracranial lesions have been formulated.
- 4. Introduction and routine use of a protocol for working with neuronavigated needle biopsy in surgical interventions of patients with supratentorial intracranial lesions.
 - 5. Evaluation and retrospective analysis of the efficacy of neuronavigated needle biopsy.

Conclusion: The presented dissertation meets the requirements of the Regulations for the development of the academic staff at the University Hospital "St. Marina", of MU "Prof. Dr. P. Stoyanov" Varna. The dissertation contains significant applied and practical scientific contributions and is worthy of awarding the educational and scientific degree "Doctor" to its author. I give a

positive assessment and vote "yes" for the award of the educational and scientific degree "Doctor" in the scientific specialty "Neurosurgery" to Dr. Martin Nikolaev Moynov.

31/05/2022 Reviewer: