STATEMENT

By Prof. Dr. Hristo Georgiev, MD,PhD,DSc.
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Subject: defense of the dissertation of Dr. Biser Aleksandrov Makelov, entitled **"One-stage Locked Externalized Stabilization In The Treatment Of Unstable Proximal Metadiaphyseal Tibial Fractures"** for the award of the educational and scientific degree "Doctor", with thesis supervisor Prof. Dr. Dimitar Raykov, M.D., Ph.D., DSc.

By the order of the Rector of Medical University of Varna № R- 109-511 / 29.11.2021 I was appointed as a member of the scientific Jury and by the decision of the latter (Protocol №1 of 30.11. "Health and Sport" in professional field 7.1 "Medicine" and doctoral program in "Orthopedics and Traumatology".

Topic Relevance: Based on clinical material and a generated three-dimensional biomechanical simulation model using the finite element method, a method of treatment of unstable tibial fractures with metadiaphyseal localization based on the principles of biological fixation is analyzed. The method is based on the application of indirect reduction techniques and definitive metadiaphyseal tibial stabilization with an externally placed locking plate. The relevance of the work is significant due to the fact that it is the first in Bulgaria to address the problem in such a scientific format. The dissertation presents the authors' views on the indications (inclusion criteria), limitations, contraindications (exclusion criteria) of the method and the choice between it and open reduction and internal fixation with angle-stable plates, locking nails and staged treatment. The medical-social relevance of the thesis is determined by the severity of the pathology, as a rule in the setting of polytrauma leading to a life-threatening condition that does not allow extensive and prolonged surgical interventions. The method under consideration is aimed at minimal invasiveness with a simplified surgical technique leading to biological bone healing, early limb mobilization and loading, and improved patient quality of life.

Compliance with Article 61(3).1.of the Regulations for the Development of the Academic Staff at MU-Varna - "Requirements for a Dissertation for the Acquisition of a PhD". The dissertation is presented according to the usual structure for this type of theses in 178 pages, 20 tables and 83 figures (which include the graphs). It includes an introduction (4 pages), a literature review (46 pages), a bibliography (10 pages with 8 titles in Cyrillic and 171 in Latin). In the remainder of the dissertation,

Dr. Makelov articulates the purpose and resulting four objectives, the study's contingent, the clinical methodology of the study and the surgical technique and postoperative protocol used, the treatment, the authors' own results, analysis, and conclusions. The dissertation also includes 5 pages of contributions, a list of own publications on the subject and acknowledgements. The latter I accept as a departure from the requirements for a dissertation. Their place is in the abstract.

The **literature review** is extensive enough. It covers all aspects of the problem while not exceeding 30% of the work. In a logical sequence, the dissertation presents the surgical anatomy of the tibia and the covering soft tissues, the biomechanics and mechanism of injury, the biology of primary and secondary bone union, the clinical and imaging diagnosis, classification systems and epidemiology of the fracture, and known treatment modalities and also the complications. Of particular interest to me personally was the section devoted to the complex interaction between the mechanical environment and cellular repair processes at the fracture site. The literature review is specific to the dissertation and is a synthesis of Dr. Makelov's extensive knowledge on the problem. This chapter can be taken as a short contemporary course refreshing our knowledge of fracture treatment and the methods of different types of fracture fixation options. The review thus, makes a significant methodological contribution to specialty training. As a criticism of the literature review, I can point out the lack of a brief analytical summary at the end of the proven, unresolved and theoretically plausible facts of the problem.

Chapter III contains the aim and objectives. The aim is clearly formulated - "To investigate the feasibility and evaluate the results of the application of one-stage locked externalized stabilization with angle-stabled plates in the treatment of unstable metadiaphyseal tibial fractures". The four objectives are specific, clear, well defined and fully consistent with the stated aim.

Chapter IV contains the methodology and clinical material.

The dissertant used a series of surgically treated patients with unstable tibial fractures in the period 2013 - 2021 in the orthopaedic department at the University Hospital "Prof. Dr. Stoyan Kirkovich AD", Stara Zagora. Based on 10 well-defined inclusion criteria (of which three were relative) and 8 exclusion criteria, surgery was performed in 26 patients. 18 patients were followed up for up to 60 months, which is the contingent of the thesis.

The mean age of the study participants was 51 years, with the youngest patient being 22 years old and the oldest 85 years old, in 83% male. The injuries were mainly from road traffic accidents and altitude trauma. According to the localization of the fractures, the most frequent fracture was the fracture of the proximal metadiaphysis - 12 pts. (with intra-articular component -7), followed by distal metadiaphysis - in 6 pts. The soft tissue injury, according to AO IO, is distributed in grade 2 – 10pts,

grade 3 - 6 pts and grade 4 - 2 pts. In 11pts. the fracture was open. The statistical treatment of the reported parameters was correctly presented in clear graphs.

In all patients, the diagnosis was made on the basis of clinical orthopaedic examination and imaging studies, i.e., orthogonal x-rays of the affected limb, with knee and ankle joints, and CT scan in complex, intra-articular fractures type 41C2 according to AO/OTA, to exclude impaction and fragmentation. The dissertant notes the importance of the angiographic study but does not provide data on how many patients it was performed in.

This chapter systematically presents the preoperative preparation and operative technique, the choice of the plate and the technique of its application. This is of great practical value to any orthopaedic trauma surgeon. The focus is on operative intervention within the first 24 hours of trauma, after stabilization of the patient's general condition. Different types of osteosynthesis devices were used: in 9 pts. - LISS DF for left or right femur with 9, 11 or 13 holes, in 2 pts. - LISS DF for left or right femur with 9, 11 or 13 holes. - LCP - broad/narrow with 12, 14 or 16 holes, , in 1pt. - LCP-PT – a contralateral(opposite) plate with 9 holes and LISS DF - contralateral plate with 11 holes in 6pts.

A protocol of postoperative treatment and follow-up with x-rays taken up, at the third, the sixth and the twelfth week, and then at two month intervals is presented. Controlled partial weight-bearingb(PWB) began most often after the 2nd postoperative day and full WB by the 12th postoperative week. Standard thrombo- prophylaxis is performed in all patients.

In my opinion, unnecessary, in this chapter, are the analyses and commentaries on literature data, e.g. Rowe et al. 2000, Goodship, 1998, et al. The place of these authors' interpretations is in the discussion.

In processing the results, the candidate applies credible modern statistical methods used in the biomedical sciences. These are presented in a separate **chapter V**, follow-up, documentation and statistics. This author's view is incorrect because these are methods and should be in the previous section.

For the purpose of this thesis, a biomechanical virtual computational finite element model has been developed in collaboration with AO Research Institute, Davos. Differences in the effect of one standard internal and two different external fixations with a LISS DF metaphyseal locking plate on the construction stability and interfragmentary motion (IFM) at the fracture zone of a unstable, proximal tibial fracture were simulated. Three different groups with different plate-bone offset were modeled for comparison. The parameters monitored in the simulation were: construct stiffness(CS), IFM and longitudinal deformation(strain) at the fracture zone. The conclusion from the experimental model is " ... In terms of virtual three-dimensional biomechanical modeling, the locking one-stage external stabilization in unstable proximal tibial fractures with a simulated thin and thick soft tissue

envelope, creates favorable biomechanical conditions for callus when the amount of longitudinal strain in the fracture zone, do not exceed 10% and provides optimal relative stability necessary for the onset of secondary bone healing under controlled PWB in the early postoperative rehabilitation period"

The results of the experimental part and the clinical series of the study are correctly presented in **Chapter VI**. Functional assessment was performed using the HSS assessment systems for the knee joint and the AOFAS for the ankle joint. The time for bone union and the intraoperative duration were selected for clinical evaluation. The patients included were divided into groups according to: age - up to 50 and over 50 years old; tibial locus - proximal or distal metadiaphysis; **simple** - multifragmentary metadiaphyseal without joint involvement and **complex**, compound with simple(without fragmentation and intra-articular comminution) joint involvement and multifragmentary metadiaphyseal tibial separation; degree of soft tissue damage – from mild to severely injured soft tissue envelope. I can summarize the results obtained:

- The HSS score performed 4 weeks after surgery and at the final examination was not statistically significantly different between patients under and over 50 years of age, in patients with proximal or distal fractures, in patients with mild and severe soft tissue injury and was e statistically significantly higher in patients with simple (A, B) fractures compared to patients with complex (C) fractures ($P = 0.04$) at 4 weeks.
- Knee extension range of motion measured at 4 weeks postoperatively and at final follow-up was not statistically significantly different in any of the groups followed.
- Knee flexion range of motion measured 4 weeks after surgery was statistically different, greater in patients younger than 50 years of age at final examination and less in patients with proximal fractures compared with patients with distal fractures.
- Functional assessment of the ankle joint was not statistically significantly different between patient groups at any of the time follow-ups.
- Range of motion in dorsal ankle joint flexion measured both 4 weeks after surgery and at the final follow-up examination showed no statistically significant difference in all four groups.
- Range of motion in plantar flexion of the ankle joint was greater in patients younger than 50 years of age at 4 weeks.
- Healing time was not affected by age and fracture location but was statistically significantly shorter in simple fractures.
- Intraoperative time was not statistically significantly different between groups and ranged from 20-45 min.

Three more significant complications are correctly presented: refracture without osteosynthesis breakdown corrected with autosteoplasty and reversed dynamization with plate in situ, septic arthritis, and subsequent knee extension contracture, due to infection along the course of the cannulated screws and severe concomitant soft tissue trauma and varus deformity with mild antecurvation in the fracture zone, with subsequent flexion contracture in the knee joint of 15° and shortening of the lower limb over 1. 5 cm. I believe that it was necessary to separate the complications into a separate subsection and classify them, e.g., according to the Clavien-Dindo classification for surgical complications. I accept this as a shortcoming of the work, but it does not alter the scientific value of the thesis.

In the chapter, the dissertation also presents seven clinical cases. These are documented with highly informative photographs adequate to the results presented.

Chapter VII - "Discussion" has a volume of 27 pages, presents an extensive comparative analysis of the candidate's view and results on the subject under discussion with those of other authors, who have worked on the problem. In general, the discussion is directed as a proof of the advantages of the one-staged locked externalized stabilization used in the fractures considered.

This chapter is the most creative part of the thesis. It convincingly demonstrates Dr. Makelov's high erudition on the presented issues. Personally, I found it the most interesting.

The discussion concludes with an assessment of three major shortcomings of the study - the small number of patients indicated for inclusion, the relatively short follow-up period, and the lack of a control group of patients treated by standard methods, necessary for comparison and evaluation of the final results.

Five important implications for practice are drawn in **Chapter IX**. With these author's conclusions and the 9 advantages and 3 disadvantages of the one-stage locked externalized stabilization presented, I fully agree and confidently accept that the stated aim of the dissertation has been fulfilled by them.

The bibliography presented in **Chapter X** is in alphabetical order.

Overall, the dissertation is written in correct literary language. The graphs and photographs used are of high quality and informative, fully appropriate to the text. The remarks I have made are methodological in nature and do not detract from the scientific value of the work.

To the scientific work of dr. Biser Makelov submitted to me for review, I can point out the following major contributions. They have a theoretical, surgical practice-oriented and confirmatory character:

1. This is one of the few dissertations in orthopaedic science using an experimental model. The developed three-dimensional computational biomechanical model provides a scientifically sound conclusion, regarding the favorable biomechanical conditions for indirect bone healing by locked one-stage externalized stabilization in unstable metadiaphyseal tibial fractures.

2. For the first time in the country a follow-up of locked one-staged externalized stabilization in the surgical treatment of unstable tibial fractures was performed, and objective advantages and disadvantages were derived. The dissertation series is one of the largest presented in the specialized literature.

3. The follow-up of patients treated according to precise indications for surgical treatment, makes it possible to derive a feasible, one-stage, low-risk, easy, practical, operative methodology for multiple trauma injuries.

On the dissertation topic, the candidate submitted three publications, seven presentations and one project, and meet the requirements of Annex 1 of the Regulations for the Development of Academic Staff at MU-Varna. They contain separate parts of the developed material.

The 62-page, abstract of the dissertation submitted to me is formatted according to the generally accepted requirements.

In conclusion, the dissertation submitted to me for review shows the dissertant's ability to pose a scientific thesis, methodology for its solution, his ability to select and process material, as well as to draw statistically reliable conclusions on a new topic for the bulgarian bone and joint surgery - one-staged locked externalized stabilization. The dissertation fully meets the qualitative and quantitative criteria set out in the Requirements for a dissertation for the degree of Doctor of Education and Science of the Regulations for the Development of Academic Staff at MU-Varna.

Therefore, **I give my positive assessment of the work** and I suggest the esteemed scientific jury formed by order R-109-511/29.11.2021 of the Rector of MU-Varna, **to award positive Dr. Biser Aleksandrov Makelov** with educational and scientific degree "DOCTOR" in the scientific specialty "Orthopedics and Traumatology".

15.12.2021

Prof. Dr. Hristo Georgiev, MD, PhD., DSc.

To the first time in the country a follow-up of locked one-staged extramedullary stabilization in the surgical treatment of unstable tibial fractures was performed, and objective advantages and disadvantages were derived. The dissertation work is one of the largest presented in the specialized literature.

The follow-up of patients treated according to precise indications for surgical treatment makes it possible to derive a feasible, one-stage, low-risk, easy, practical, operative methodology for multiple trauma patients.

On the dissertation topic, the candidate submitted three publications, seven presentations and one project and met the requirements of Annex 1 of the Regulations for the Development of Academic Staff at MU - Varna. They contain separate parts of the developed material.

The defense abstract of the dissertation submitted to me is formatted according to the generally accepted requirements.

In conclusion, the dissertation submitted to me for review shows the dissertant's ability to pose a research thesis, methodology for its solution, his ability to select and process material, to analyze it, draw distinctly reliable conclusions on a given topic for the delegation in the educational-qualification degree "doctor" in the scientific specialty "Dentistry" at the Medical University - Varna.

Therefore, I give my positive assessment of the work and I suggest the scientific jury presented by order P-1099/01.12.2021 of the Rector of MU-Varna to award to Dr. Nikolay Vladimirov Nikolov with educational and scientific degree "DOCTOR" in the scientific specialty "Orthopedic Dental Treatment".

15.12.2021 Prof. Dr. Hristo Georgiev MD, DSc