REVIEW

by

Assoc. Prof. Dr. Georgi Konstantinov Poptodorov, PhD
Department of Neurosurgery UMHSTEM "N.I. Pirogov".

Member of a scientific jury based on: Art. 32, par. 2 and 3 of the Regulations for the Development of the Academic Staff at UMBALSM "NI.Pirogov", Sofia and according to the decision of the Academic Council with protocol No. ND-01-2/18.05-2022 and based on Order No. RD - 26-1325/30.05.2022 of the Executive Director of UMHATEM "N. I. Pirogov ",

Regarding: Dissertation work for the acquisition of the scientific degree "Doctor of Medical Sciences" in the scientific specialty "Neurosurgery"
of Assoc.Prof.Dr. Nikolay Svetoslavov Yanev, PhD

Mailing address:
Neurosurgery Department - UMBALSM "N.I. Pirogov"
Bul. Totleben №21, 1606 - Sofia.
Tel.: 029154294; Mob.: 0888638613;
Email: gpoptodorov@gmail.com

A dissertation work of Nikolay Svetoslavov Yanev, Ph.D., PhD, entitled "Algorithm for clinical application of virtual planning, modeling and 3D printing in local, regional and microvascular reconstructions of complex maxillofacial defects" is presented for review

Biographical data of the candidate

Born on 07.05.1976. Secondary education graduation in 1994. After completing military service, graduated in stomatology (Dental Medicine), obtaining a Master's degree in 2002. In 2010, he also obtained a Master's degree in Medicine at the Faculty of Medicine, MU - Sofia.

Professional development

of Associate Professor Nikolay Svetoslavov Yanev began in 2003.
Since then, he has specialized in "Maxillofacial Surgery" at the Military Medical Academy - Sofia and SHAT for MFS.

He has specialized in Great Britain (Head and Neck Department, University College London Hospital NHS Foundation Trust (07.2012–04.2013) and Head and Neck Department, Royal Derby Hospital. (04.2013–07.2015).

MFS Specialty defended in 2012. Since 2013, he has a recognized specialty in oral and maxillofacial surgery in Great Britain; Fellow of the European Board of Oral and Maxillofacial Surgery (FEBOMFS) - 2018

The candidate attended 33 professional qualification courses for the period 2007-2020, mainly in Great Britain, but also Germany, Belgium, Austria and Ireland.

He worked as a specialist maxillofacial surgeon at the Specialized Hospital for Maxillofacial Surgery - Sofia (08.2015–09.2019) and Head and Neck Department, Royal Derby Hospital, UK. for the periods 02.2016 - 03.2017 and 04.2017–04.2018.

He has a recognized doctoral degree for a defended dissertation on the topic: "Mechanism-directed treatment of pain - experimental models and pharmacological effects", developed in the Department of Pharmacology and Toxicology of the MU - Sofia. He was habilitated in

2016, being successively Associate Professor at the Scientific Research Institute of the MU – Pleven (12.2016–03.2018), Associate Professor at the Department of Pharmacology and Toxicology, MU – Pleven 04.2018–12.2019 and Associate Professor and Head of the Department of Pharmacology , UMBALSM "N.I. Pirogov" 10.2019–05.2022

Scientific publications

The candidate has 35 scientific papers for the period 1998 - 2021 (in 10 of them he is the first author). His publication activity demonstrates diverse interests. The largest number of actual publications – 17 – are devoted to various aspects of the study of pain. There are 10 contributions to textbooks and monographs - in 5 of them he is the first author. Associate Professor Yanev has presented his participation in scientific forums - congresses and conferences - a total of 28 of which there is one participation in a world forum (29-th World Congress of the International College for Maxillofacial Surgery), in 4 European and in a number of international and regional scientific events .

Dissertation work

The material "ALGORITHM FOR CLINICAL APPLICATION OF VIRTUAL PLANNING, MODELING AND 3D PRINTING IN LOCAL, REGIONAL AND MICROVASCULAR RECONSTRUCTION OF COMPLEX MAXILLOFACIAL DEFECTS" consists of 246 pages with 12 tables and 147 figures. The paper is also presented in digital format.

Note: As noted in the abstract, the numbers of the tables and figures do not correspond to the numbers in the dissertation. The numbering in this review follows that used in the dissertation

The radical surgical treatment of diseases of the face and neck presents a serious challenge. In large part, the need for surgical treatment is required due to the development of oncological suffering. Radicality is limited on the one hand due to the anatomical presence of a large number of important functional structures, and on the other hand due to the fact that large-scale surgical resections cause serious cosmetic defects. The combination of soft-tissue plastic

reconstruction using free flaps with reconstruction of the underlying facial skeleton using custom-made 3-D printed implants is about to become the standard in the treatment of craniofacial defects. The concept is applicable to both oncological diseases and defects of an inflammatory, traumatic or dysembryogenetic nature.

The aim of the methodology is not only to remove the pathological process, but also to achieve a simultaneous functional and aesthetic recovery. The challenges posed by the planning, organization and implementation of such an intervention are many, and the insufficiently accumulated experience not only in the country but also on a global scale is of essential importance. Systematic research in this area has not been done in Bulgaria, and in this regard the developed study is a pilot study for the country. The organization of multidisciplinary medical teams, as well as the performance of individual engineering and production activities for each patient, presuppose high qualification and broad knowledge. The creation of an effectively working team trained according to international standards is a challenge, which is why the topic is relevant not only from a scientific point of view, but also from a teaching and organizational-methodological point of view.

The submitted work is properly structured according to the academic requirements. It is noteworthy that at the end of the scientific work there is no description of the contributions. Such a description can be found in the dissertation abstract and has been used for this review.

A table of the used abbreviations is presented in an overview.

Literature review

After a short introduction, the author presents an overview of the available literature on the topic. The literature review (pp. 6-82) begins with an introduction to the history of facial reconstruction and the first attempts to introduce regional arterialized flaps in the late 1960s. The following is a description of the literature and current issues of microvascular surgery.

The review shows the good knowledge of the author and his thorough research of the available literature.

As a shortcoming in the next section, I will point out the lack of cited literature sources in the sections "Optical Magnifying Equipment for Microvascular Surgery" and "Illumination in Microscopic Systems" For the section "Regional Vascular Anatomy of the Face and Neck" there are only two cited sources.

The main part of the literature review (pp. 29-56) is devoted in detail to tissue flaps. The survey covers the majority of contemporary publications on the subject, not neglecting classical sources. In the next part, the history of the development of microvascular and digital-assisted reconstructive facial surgery in Bulgaria is examined in detail. Logically related to the topic, the literature review continues with a description of the history, evolution and modern achievements in virtual planning, modeling and 3-D printing in medicine and in particular the problem under consideration. Much attention has been paid to the medical engineering aspect, as well as to the production process for the main materials used for 3D printing.

The author defines, as the Objective of the work presented for review - "Creation of an algorithm for clinical application of the methods of virtual 3D planning, modeling and printing in local, regional and microvascular reconstructions of extensive bone defects in the maxillofacial area, after carrying out the relevant surgical treatment and follow-up of its results."

The aim of the dissertation is precisely and concretely formulated and the tasks are defined in a logically correct order, starting with the systematization of the available knowledge and experience on a national and global scale. This preparatory part is of particular importance when developing topics that are new to medicine and where a number of high-tech modern engineering methods are applied. Tasks #2 and #3 are hands-on interdisciplinary medical-engineering activities that fully cover the process from digital planning to manufacturing 3-D patient-specific implants. The clinical application in practice is reflected in the set task #4. The tasks are correctly arranged, because in the process of carrying out the research and

introducing these new methods, the candidate analyzed the scientific and technical aspect of the problem, gained operative surgical experience, which improved his practical training. In parallel, he has acquired the necessary organizational experience needed to lead such a complex activity carried out in one step by several teams. The last task essentially represents the achievement of the set Goal.

Material and methods

This section (pp. 84 – 108) of the scientific work is presented in detail and comprehensibly. The description of the clinical material and the methods used is textually precise and well illustrated.

The material is based on the data from a series of 22 consecutive patients. The study covers a 4-year period. The duration of the study, the number of analyzed cases and the short period of clinical observation are not an obstacle to the achievement of the set goal and tasks. Regionally, the study is cutting-edge, and the small number of cases selected for the study can be explained by certain socioeconomic factors beyond the scope of clinical medical practice. The material is divided into two main groups according to the type of operative technique applied. Statistical processing and analysis were performed using statistical tools that allow reliability in the study of small groups. The study is pioneering for the country and the conclusions should be further confirmed on the basis of future larger studies.

Research **methods** are properly selected and meet the objectives of the study.

The study used a wide range of clinical medical methods including operative, laboratory, instrumental and neuroimaging ones. In parallel, informational, technological and medical-engineering methods were used. Digitized images of the operative procedures performed are included. Statistical processing and analysis were professionally performed using modern statistical tools.

Results

In this section, the author presents in detail the clinical history and surgical approach in each

of the cases that are the subject of the dissertation. The presentation, which is a little unconventional for a dissertation, introduces us to the challenges of surgical work. The surgical technique demonstrated through the presented clinical cases is of a very high level and is undoubtedly the result of hard work and purposeful self-improvement. The early postoperative results presented are very promising. The clinical series was not followed up for a long period as this was not necessary for the set goal and objectives of this scientific work. To evaluate the results, it would be advisable to examine the quality of life in these patients in the long term.
The discussion of the results is presented systematically according to the set tasks.

The analysis and conclusions drawn by the doctorant as a result of the obtained results allow him to propose the introduction into clinical practice of a behavioral algorithm developed by him, which is also the purpose of the reviewed work. The developed algorithm is an auxiliary tool in making a decision - in choosing a method of behavior and for the type of appropriate technique, thus representing a practical contribution as a result of the dissertation work - implementation of comprehensive surgical treatment - digitally-assisted maxillofacial resection and/or local, regional or microvascular reconstruction of the complex tissue defect. It is noteworthy that a relatively small part of this undeniably interesting and systematized results has been published or presented at international specialized forums.

The bibliography consists of 253 literary sources. 15 of them are in Cyrillic. The literature reference is properly arranged and meets the academic requirements.

The illustrations in the scientific paper are indicative and of very good quality. For some of them, no literature source is cited, such as Fig. 2 and Fig. 3., as figure 93, which is from a published article by the author. The image in Fig. 13 is irrelevant to the scientific work.

Scientific presentations and appearances related to the habilitation work
The candidate submitted a list of "Publications and participation in scientific forums in connection with the dissertation work" The list contains 15 scientific publications and 5 participation in scientific forums.

Scientific publications. The presented publications were issued before 2007 - 1 item. ; 2009 – 3 pcs. (Chapters from a textbook on Dental medicine III course - Oral medicine. (Edited by Z. Krastev, A. Kiselova, R. Kolarov); 2013 -1 issue; 2014 -1 issue; 2016 - 2 No. (chapters from the monograph "Biocompatibility in oral medicine. From theory to practice. (Edited by A. Kiselova, B. Petrunov"); 2019 -2 nos.; 2020 -3 nos.; 2021 . - 2 pcs.

Six of them are in English. The presented publications thematically touch on a wide range of issues. Publications No. 1, No. 6, No. 7, No. 9, No. 13, No. 14, as well as No. 11, No. 12, dealing with the issues of implant application and their biocompatibility, are directly related to the topic of the scientific work. Publications #4, #8, #15 are devoted to loco-regional anesthesia, pharmacology and pain mediation, and #3 and #5 to related facial developmental defects. Publication No. 2 has an indirect relation to the problems that are the subject of the scientific work.

Participation in scientific forums in connection with the dissertation work (2016-2018) is entirely dedicated to the topic. The first three were presented at forums of regional importance and the other two at the 24th Congress of the European Association for Cranio-Maxillo-Facial Surgery, 2018 Munich, Germany

The scientometric indicators are as follows:

Yanev N, Blagova B, Andreeva L. Unusual Impaction – Rosettes of Multiple Unerupted Molars: Review Article. International Journal of Dental Medicine (IJDM). 2020; 6(1): 1–6	International Journal of Dental Medicine (IJDM). IF - 0.1 extended IF - 2 SJR - (2020) N/A
Blagova B, Yanev N. Two – versus one stage inferior nerve block – is there a difference in the application	Acta medica Croatica, SJR – (2020) -0.102

pain levels? A prospective clinical study. Acta medica Croatica, 2020; 74(4): 329–335.	
Yanev N, Malinova A, Yordanova G, Markov D. Regional reconstructions facilitated by a 3D modelling in oral cancer cases involving mandible. A look into surgical time, cost and clinical features. British Journal of Oral and Maxillofacial Surgery. Dec. 2019; 57(10): e40–e41,	British Journal of Oral and Maxillofacial Surgery. Impact Factor (WoS) 1.651; SJR (2019) - 0.529

Abbreviations

IF - Impact Factor

SJR - - SCImago Journal Rank

WoS - - Web of Science

The contributions presented as a result of the study are original not only from a clinical but also a production-technical point of view. On the other hand, the presented work has a methodological and practical significance, since the author presents his generalized clinical experience in the light of modern scientific and technical achievements. It should be noted the very good presentation of the "Operational methods" section, which has a number of practical organizational-methodical tips and represents a propaedeutic contribution to this scientific work.

In conclusion: The work submitted for review is a well-prepared and completed study of a specific and topical practical problem. The doctorant has shown comprehensive theoretical and practical knowledge and an analytical approach and has fulfilled the goal he set for himself. The published materials are original and reliable, with minor remarks they are

presented in an overview and are critically discussed. The developments and results have cutting-edge practical contributions to the country and can be the basis of larger-scale studies in this area. The scientific work covers the mandatory indicators and criteria laid down in the LDASRB in its Regulations for its implementation, as well as in the Regulations for the development of the academic staff of UMHATEM "N.I. Pirogov", Sofia.

Due to the above, I give a positive assessment to the peer-reviewed work of Dr. Nikolay Yanev, PhD on the topic "Algorithm for clinical application of virtual planning, modeling and 3D printing in local, regional and microvascular reconstructions of complex maxillofacial defects" and suggest to the scientific jury to be awarded the scientific degree "Doctor of Sciences"

Sofia 03. July. 2022 r.

With respect

Assoc.Prof.Dr.Georgy Poptodorov, PhD