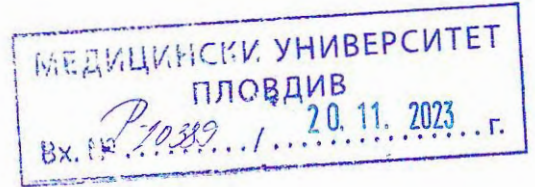


To the **Chairman** of the Scientific Jury
designated by Order No. № P-3317/15.11.2023
of the Rector of the Medical University of Plovdiv.

REVIEW



by **Prof. Dr. Rosen Gospodinov Kolarov, PhD,**
Medical University of Varna, Faculty of Dental Medicine,
Department of General and Special Surgery
of a dissertation for receiving
a doctoral degree

Sphere of higher education:

7. Healthcare and sports

Professional field:

7.2. Dental Medicine

Doctoral programme: Scientific speciality: Oral Surgery – 03.03.04

Author: Nikolay Dimitrov Kanazirski, DMD

Self-training **PhD student** at the Medical University of Plovdiv

Department of Oral Surgery of the Faculty of Dental Medicine at the Medical University of Plovdiv

Theme:

**Er:YAG Laser Implant Site Preparation for Placement of Dental Screw Implants:
Clinical, Histological and Morphological Studies**

Academic supervisor: Assoc. Prof. Dr. Deyan Zdravkov Neychev, PhD – Department of Oral Surgery of the Faculty of Dental Medicine at the Medical University of Plovdiv

1. General Presentation of the Procedure and the Doctoral Candidate

This review has been prepared based on Order of the Rector of the Medical University of Plovdiv № P-3317/15.11.2023, with appointed Scientific Jury under the procedure for public defence of the aforementioned dissertation.

The presented set of materials, both in paper and electronic formats, is in compliance with Art. 115 (1) of the Procedure for Awarding Doctoral Degrees at the Medical University of Plovdiv, set in the Regulations of the Medical University of Plovdiv of 06 Nov 2014, and was provided to me within the legal time period.

The doctoral candidate submitted three publications and two participations in international congresses related to the dissertation's theme.

All materials were meticulously prepared and presented.

2. Biographical Notes of the Doctoral Candidate

Dr. Kanazirski was born on 09 Oct 1961.

He graduated from the Faculty of Dental Medicine at the Medical University of Plovdiv in 1986, obtaining a master's degree in Dental Medicine. He graduated with full honors.

Since 1989, Dr. Kanazirski has held positions as an assistant professor and chief assistant professor at the Department of Oral Surgery of the Faculty of Dental Medicine - Plovdiv.

He acquired a specialty in Oral Surgery in 1993.

In 2005, he acquired a specialty in General Dentistry.

In 2021, he acquired a specialty in Dental Implantology.

Dr. Kanazirski has more than 30 participations in national and international scientific congresses and conferences and more than 20 publications in referenced journals and journals with an impact factor.

Dr. Kanazirski is a member of:

- the Bulgarian Dental Association (BDA)
- the Bulgarian Scientific Society of Dental Medicine (BSSDM).

He has a good command of Russian and German, both written and spoken.

3. Significance of the Theme and Appropriateness of the Objectives and Tasks Set

The dissertation's theme addresses a significant issue in medical science and practice. The objective is clearly stated, the tasks are defined correctly and have been implemented using modern research methods.

4. Understanding of the Issue

In his dissertation, Dr. Nikolay Kanazirski shows in-depth knowledge of the theme.

Restoring the function and esthetics of the dentition has become completely possible in modern dentistry, thanks to the major advancements in dental implantology. Placing dental implants has become a routine procedure. A thorough understanding of the mechanisms of osseointegration is essential to achieve positive outcomes in implantological treatment. Modern dentistry faces the challenge of providing superior quality of the end result. Rapid treatment results within a short period without complications are needed for patient satisfaction.

The placement of dental screw implants typically involves the use of rotary technique to create a bone bed for implant placement.

Dr. Kanazirski has made a thorough critical analysis of the literature on the subject. In this analysis, he emphasizes that among the possibilities for influencing the various factors determining the mechanisms of osseointegration, the treatment possibilities of Er:YAG lasers are underexplored. When using such lasers to make an osteotomy, a lot of time is wasted. Other disadvantages are the inaccuracies in the diameter and length of the cavity, carbonization of the bone in the depth of the implant site, etc.

The other option available is to remove the smear layer using an Er:YAG laser. This method is used in the practice. However, no thorough study of the mechanisms improving osseointegration is available. The combination of conventional rotary techniques and laser demonstrates synergistic effects, making it possible to prepare a cavity with precise dimensions, to eliminate the smear layer and remove the bacterial biofilm.

Dr. Kanazirski has demonstrated his ability to conduct research independently. The exposition is written in a good scientific language.

Based on the analysis of the scientific research carried out so far on the issue, the objective of the scientific work was formulated, namely:

“The objective of this study is to assess the dynamics in the process of osseointegration with Er:YAG laser treatment of the implant site.”

5. Methods

To achieve this objective, Dr. Kanazirski set four main tasks and two subtasks, namely:

1. Task 1: Comparison of experimental mandibular osteotomy analogues in four groups by means of histomorphometric studies.

2. Task 2: Comparison of experimental mandibular osteotomy analogues in two groups by scanning electron microscopy (SEM) study.

3. Task 3: Studying osseointegrable screw implants in patients placed in a cavity treated by an original method using an Er:YAG laser using resonance-frequency analysis. Monitoring and evaluation of the healing process based on the data obtained.

3.1. Assessment of the primary and secondary stability (at month 3) of screw dental implants with closed implantation method in 30 patients.

3.2. Following-up the dynamics of the healing process and osseointegration in 15 patients with an open implantation method. Assessment of the primary stability, the stability on day 10, 20 and 30, and the secondary stability.

4. Task 4: Developing an algorithm for placement of osseointegrable screw implants in bone beds whose surface is treated with an Er:YAG laser using an original method. Registration of a useful model “Modular Complex for Site Preparation for Placement of Spiral Dental Implants” at the Patent Office of the Republic of Bulgaria.

Study Design

The study includes an experimental part conducted on 10 domestic pigs (*Sus scrofa domestica*). 50 sections were prepared and examined by histological analysis and electron microscopy, and a large number of permanent slides with horizontal and vertical sections were prepared, Carrying out scanning electron microscopy (SEM).

The study also includes a clinical part conducted in 30 patients.

Study site:

The study was conducted at the Department of Oral Surgery at the Faculty of Dental Medicine of the Medical University of Plovdiv; the Section of Technology of Dosage Forms and Biopharmacy of the Department of Pharmaceutical Sciences at the Faculty of Pharmacy of the Medical University of Plovdiv; the Department of Veterinary Anatomy, Histology and Embriology of the Faculty of Veterinary Medicine of the Trakia University in Stara Zagora; the Dental center "Easy Dent" - Plovdiv.

Study period:

The study was conducted over a period of one year. The results were recorded in a clinical statistical chart specially designed for the project.

6. Material**Material for Task 1.**

Mandibles from 10 domestic pigs (*Sus scrofa domestica*) were examined, and 50 osteotomies were made using standard drills.

Comparison of experimental mandibular osteotomy analogues in four groups by histological analysis.

Group A - cavity prepared with standard implantology drills.

Group B - cavity prepared with standard implantology drills and surface treatment of the implant cavity walls with an Er:YAG laser;

Group C - cavity prepared with standard implantology drills and implant placed.

Group D - cavity prepared with standard implantology drills and surface treatment of the cavity walls with an Er:YAG laser; implant placed.

Histological analysis of mandibles from 10 domestic pigs (*Sus scrofa domestica*) was carried out.

Material for Task 2

Comparison of experimental mandibular osteotomy analogues in two groups using scanning electron microscopy (SEM). SEM study methodology.

1. An innovative approach – using an Er:YAG laser to treat the implant site surface by the aforementioned method – was applied.

2. The samples were examined using SEM.

Structural and morphological changes in bone tissue surfaces after trepanation with standard drills and after laser treatment were investigated using scanning electron microscopy (Prisma E SEM, Termo Scientific, Waltham, MA, USA). The scanning electron microscope is equipped with a thermal emission SEM column, a CCD camera, and a multi-purpose sample holder for 7 stubs. The samples were examined at an accelerating voltage of 10 kV and several magnifications (65x, 120x, 350x, 800x), using a low-vacuum detector (LVD).

The investigations were carried out at the Section of Technology of Dosage Forms and Biopharmacy of the Department of Pharmaceutical Sciences at the Faculty of Pharmacy of the Medical University of Plovdiv.

Material for Task 3

Assessment of the primary and secondary stability of osseointegrable screw implants in patients at month 3.

Thirty patients over the age of 18, in good general condition, without severe concomitant diseases and without taking medications preventing surgical procedure, were studied.

The persons studied had extracted teeth of the mandible - premolars or molars, with the extraction performed more than six months earlier, unilaterally and bilaterally. Patients with sufficient bone volume in the premolar area and less bone thickness in the molar area, necessitating the use of implants with a diameter of up to 4.2 mm and a length of up to 11.5 mm, were selected. There should have been no need for bone augmentation for implant placement.

30 implants were placed and the patients were followed-up over a period of one year.

The study findings were recorded in a clinical statistical chart specially designed for the project.

Material for Task 4

To develop an algorithm for placement of screw implants in bone beds whose surface is treated with an Er:YAG laser using an original method. An useful model "Modular Complex for Site Preparation for Placement of Spiral Dental Implants" was registered at the Patent Office of the Republic of Bulgaria.

Statistical Methods for Data Analysis:

The study was conducted with the personal participation and control of the doctoral candidate.

The number of logical units is sufficient for making conclusions of good scientific value.

The systematization, processing and analysis of the primary data in the form of quantitative and qualitative variables were performed with IBM SPSS Statistics (Statistical Package for the Social Sciences) v. 26. A significance level of $\alpha = 0.05$ was used for all tests. The analysis, conclusions and recommendations from the study were formulated after the summarized presentation of the empirical results in tabular form and are illustrated with their corresponding graphic images. Graphical analysis was performed in an MS Office 365 environment using Excel.

The following statistical and mathematical methods were used to objectify the results of the conducted analyses:

1. Descriptive analysis to describe the structure of the studied variables
 - Descriptive statistics for quantitative variables – quantitative description of the main parameters and characteristics of the dataset, generalization and assessment of the main statistical parameters. Normally distributed data are presented as mean \pm standard deviation (SD), while in the absence of normal distribution, the data are presented by positional averages - median (Me) and interquartile range (IQR) or 25th and 75th percentiles.
 - Descriptive statistics for qualitative variables - absolute and relative frequencies. They are presented as simple numerical values (n) and as a relative proportion (%), respectively.
2. Statistical hypothesis testing
 - parametric analysis:
 - one-way analysis of variance ANOVA - to compare the means of three or more independent (unrelated) groups;
 - non-parametric analysis:
 - Shapiro-Wilk test – to check consistency between empirical and theoretical distribution.
3. Graphical analysis - boxplot

The results of the conducted analyses were presented through frequency tables (multidimensional tables of the frequency distribution), containing:

- absolute frequencies- the number of items in an individual group;
- central tendency measures and dispersion measures
- relative frequencies - the number of items in an individual group divided by the total number of items in all groups.
- p-values

7. Characteristics and Evaluation of the Dissertation

The dissertation meets the requirements for dissertation according to the Rules of the Medical University of Plovdiv and the Act for the Development of the Academic Staff in the Republic of Bulgaria. It spans on 153 pages. It includes 25 tables and 38 figures, three appendices, 332 references, of which 3 using Cyrillic alphabet, and 229 using Latin alphabet.

The results are comprehensively and correctly described, analyzed and interpreted.

The discussion follows the same sequence as the order of results. After each task, there are logically arranged conclusions. Conclusions are specific and summarize the results related to the main and most important aspects of the work.

The conclusions drawn after discussing the results are as follows:

1. The histomorphometric studies performed indisputably prove the effectiveness of the Er:YAG laser with a wavelength of 2940 nm, in the proposed mode of operation, for the reduction of the amorphous (smear) layer on the surface of the osteotomy implant site prepared with standard rotary instruments.

2. Combining the positive aspects of classical osteotomy performed with rotary instruments and subsequent surface treatment with Er:YAG laser of the implant site shows synergistic effects.

3. The study demonstrates that elimination of the smear layer and surface modification of bone with Er:YAG laser ensure higher primary stability of implants.

4. As a consequence of the reduction of the amorphous layer, the decrease in the stability of the implants between day 10 and 30 is minor.

5. The measured implant stability at day 30 is close to or equal to the secondary stability, which is a sign of rapidly developing osseointegration.

6. Preservation of high stability until day 30 gives reason to consider early, even immediate, loading of the implants with prosthetic restorations.

7. The high secondary stability measured by the resonance-frequency analysis method and recorded radiologically is proof of the excellent osseointegration of implants placed in bone beds prepared using a combination of the conventional method and surface treatment with an Er:YAG laser with a wavelength of 2940 nm.

The dissertation finishes with conclusions based on the discussion and the ensuing relationships.

Contributions and Significance of the Dissertation for the Science and Practice

Contributions of a Scientific and Applied Nature

1. For the first time in Bulgaria, a systematic study of the effect of Er:YAG laser with a wavelength of 2940 nm in the placement of dental screw implants was conducted.

2. For the first time, a combination of conventional osteotomy performed with rotary instruments and subsequent treatment of the site surface with an Er:YAG laser with a wavelength of 2940 nm was used for placement of dental screw implants.

3. The importance of the Er:YAG laser in terms of improving the process of osseointegration after placement of a screw implant was demonstrated indisputably.

4. A useful model was developed: “Modular Complex for Site Preparation for Placement of Spiral Dental Implants”. It was registered at the Patent Office of the Republic of Bulgaria under registration number 4368U1.

8. Assessment of Publications Related to the Dissertation

Three publications and two participations in international congresses related to the dissertation have been presented, with Dr. Kanazirski being the first author in all three publications and in one of the scientific communications, namely:

1. Kanazirski N, Kanazirska P. Auto-tooth bone graft material for reconstruction of bone defects in the oral region: case reports. *Folia Med (Plovdiv)* 2022; 64(1):162-8. doi: 10.3897/folmed.64.e59099.

2. Kanazirski N, Vladova D, Neychev D, Raycheva R, Kanazirska P. Effect of Er:YAG Laser Exposure on the Amorphous Smear Layer in the Marginal Zone of the Osteotomy Site for Placement of Dental Screw Implants: A Histomorphological Study. *Journal of Functional Biomaterials*. 2023; 14(7):376. <https://doi.org/10.3390/jfb14070376>

3. Kanazirski N, Neychev D, Raycheva R, Zahariev N. Laser Biomodification of the Bone Bed Surface for Placement of Spiral Dental Implants: A Study Based on Scanning Electron Microscopy. *Folia Med* 2023; 66 (1) – in press

Participation in international congresses:

1. Kanazirski Nikolay, Giragosyan Krikor, Kanazirska Petya. Application of Er-YAG laser in the preparation of bone for autogenous targeted tissue regeneration. 17th ISLD World Congress. 6-8 June, 2019, Plovdiv, Bulgaria.

2. Ivan Chenchev; Veselina Ivanova; Nikolay Kanazirski; Stefan Zlatev. Evaluation of primary and secondary stability of dental implants placed after soaked preservation with allograft or PRF- A randomized controlled clinical trial. 28Th Annual Scientific Meeting of the European Association for Osseointegration. 26-28 September 2019.

9. Personal Involvement of the Doctoral Candidate

I consider that the research conducted under experimental conditions, as well as the observations of patients and the resulting conclusions and contributions in the dissertation are personal work of the author.

10. Author's Summary

The author's summary aligns with the requirements of the Act for the Development of the Academic Staff in the Republic of Bulgaria and the regulations of the Medical University of Plovdiv. It reflects the content of the dissertation.

11. Critical Comments and Recommendations

The set of materials related to the dissertation, which was submitted to me, is complete and is in accordance with the Act for the Development of the Academic Staff and its Implementation Rules as well as with the regulations of the Medical University of Plovdiv. I have no comments or recommendations.

12. Personal Impressions

Dr. Kanazirski is an experienced oral surgeon and a sought-after doctor and teacher with long-standing experience. The dissertation presented by him is the result of his experience and his scientific research, based on his knowledge in the specialty. The text submitted to me shows a thorough knowledge of the problem and gives me reason to consider it personal work of the candidate.

13. Recommendations for Future Use of Dissertation Contributions and Results

I recommend to Dr. Kanazirski to publish his dissertation as a training aid, so that his work be more accessible to colleagues and very useful in their daily practice.

CONCLUSION

I consider that the dissertation of Dr. Nikolay Kanazirski, a self-training PhD student, themed: **Er:YAG Laser Implant Site Preparation for Placement of Dental Screw Implants: Clinical, Histological and Morphological studies**, submitted to me for review, is complete. The dissertation meets the requirements set in the Higher Education Act, the Development of the Academic Staff in the Republic of Bulgaria Act, its Implementation Rules, and the Rules of the Medical University of Plovdiv.

The theme is significant and well-chosen.

The literature review is comprehensive and gives a clear idea of the current state of the issue under consideration. It ends with a critical analysis, which is a good basis for the research carried out.

Based on the analysis of the scientific research carried out so far, the objective of the scientific work was formulated. The tasks set make it possible to prove the objective.

The studies carried out are of interest to dental and medical science and practice. I consider that the results obtained, their interpretation, as well as the presented related publications are the author's personal work.

The dissertation shows that the doctoral candidate Dr. Kanazirski possesses in-depth theoretical knowledge and professional skills in the specialty Oral Surgery, demonstrating competences and skills for conducting independent research.

Based on the above, I consider that the requirements set in the Act for the Development of the Academic Staff and its Implementation Rules as well as in the regulations of the Medical

University of Plovdiv are met. The presented materials and dissertation results are **in full** compliance with the specific requirements of the Medical University of Plovdiv.

In conclusion: Hereby, I confidently give my positive opinion of the dissertation themed **Er:YAG Laser Implant Site Preparation for Placement of Dental Screw Implants: Clinical, Histological and Morphological Studies** and I will cast my **POSITIVE** vote for awarding **doctoral degree** in the scientific speciality **Oral Surgery**, code **03.03.04**, to **Dr. Nikolay Dimitrov Kanazirski**.

17.11.2023

Reviewer:
(Prof. Dr. Rosen Gospodinov Kolarov, PhD)

