

REVIEW

from Prof. Dr. Aneliya Klisarova, MD, PhD, DSc

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Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

Re: Dissertation thesis for obtaining the educational and scientific degree "Philosophy Doctor" of **Dr. Ivailo Georgiev Hristov**, Department of Parodontology and Dental Implantology, Faculty of Dental Medicine at the Medical University of Varna entitled:

Single photon emission computer tomography with ^{99m}Tc MDP (methyl diphosphonate) of peri-implantant bone tissue during the healing period after the insertion of intraossal osteointegratable implants" in the field of higher education 7. "Healthcare and sports", professional division 7.2. "Dental medicine" and scientific specialty "Therapeutic dental medicine".

Dear members of the Scientific Jury,

By Order № R-109-140/05.04.2022 of the Rector of the Medical University of Varna I was selected to be an internal member of the Scientific Jury and write a review.

Brief biographical data

Dr. Ivailo Hristov was born in 1988. In 2013 he graduated the Medical University of Varna with excellent academic achievement. Since 2017 he has been a regular assistant professor at the Department of Periodontology and Dental Implantology, in 2020 he acquired the specialty "Dental imaging diagnostics". Dr. Hristov has an excellent proficiency in English language.

General introduction to the procedure and the PhD student

The presented set of materials in hard copy and on an electronic carrier is complete. It has been submitted within the deadline and in accordance with the Regulations for the Development of the Academic Staff at the Medical University of Varna.

Notes and comments on the documents

The structure of the dissertation thesis presented by Dr. Ivailo Hristov fully corresponds to the one required for presenting at defense – introduction, literature review, purpose and tasks, material and methods of the dissertation thesis, results and discussion, conclusions and recommendations. It covers 151 pages and is visualized with 11 tables, 26 figures and 30 photos. The bibliography includes 402 literary sources, of which 9 in Cyrillic and 393 in Latin. The bibliography is extensive and well-structured.

The dissertation summary reflects the structure of the dissertation thesis and meets the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria.

The PhD candidate has enclosed three publications related to the topic of his PhD work, published in international journals.

Topicality of the problem and purposefulness of the aim and tasks

The treatment of intraosseal osseointegratable dental implants is a modern therapeutic method by means of which overall rehabilitation is achieved, fully recovering the patient's chewing function and esthetics. The long-term follow-up in time and the accumulated research experience make the implant treatment reliable and highly predictable. The success of the implant treatment is associated with the process of osseointegration.

Osseointegration is a process of bone formation between the alloplastic material and the surrounding biological environment. Of paramount importance for this complex and multi-step healing process is the achievement of primary stability at implant placement.

The successful treatment is determined by the presence of adequate bone structure (quality and quantity), whose deficit is a major impediment for the insertion of intraosseal implants, especially in the distal regions of the upper jaw. The bone in this area is sleazy, containing mainly spongy with little quantity of compact bone.

The implants design, the characteristics of the implant surface, the quality and quantity of the bone, in which it is inserted, the applied surgical technique, the burden conditions and last but not least, the health status of the patient, have a direct bearing on the osseointegration process.

The follow-up during the healing period after the implant insertion is an important component of the treatment process, whose analysis allows us to continue with the next stage of the treatment or to postpone the burdening of the implant placed in the bone with a prosthetic construction.

Today, in the literature, a detailed and systematized analysis is lacking for the study of the osteoblast activity in the peri-implant bone during the course of the healing period, when inserting intraosseal osseointegratable dental implants.

Literary awareness

The introduction emphasizes the specific features of the implant treatment and the role of osseointegration in it as well as the significance of the monitoring during the healing period for the treatment process.

The literary review presented in the dissertation thesis is profound and encompasses 5 chapters in a logical sequence.

For the improvement of the osseointegration and the long-term success of the implants we have to take into consideration characteristics such as biomaterials, implant length and geometry, biomechanical factor, surface characteristics, patient's medical status, bone quality and the applied surgical technique. In a concrete and analytical manner Dr. Hristov presents the main accents published in literature in relation to the factors influencing the process of osseointegration and the primary stability of the implant, the investigation methods for the jaw bones and the application of single photon emission computer tomography for the follow-up of the healing period after the placement of intraosseal osseointegratable implants.

After a thorough and analytical review of the literary data and the scientific research on the topic in question, Dr. Hristov reaches the conclusion that the information on the issue is insufficient and the research on the application of single photon emission computer tomography for the monitoring of the healing period after the placement of intraosseal osseointegratable implants continue with increasing intensity worldwide. The PhD student also presents in historical sequencing the application of single photon emission computer tomography as an investigation method in dental implantology.

Aim and tasks

The aim of the PhD thesis is formulated in a clear and concrete way – to evaluate the application of single photon emission computer tomography [SPECT] with ^{99m}Tc -MDP of peri-implanted bone tissue during the healing period after the insertion of intraosseal osseointegratable implants.

To achieve this purpose, the PhD student has set 3 tasks which are also in logical sequence and correspond to the aim:

1. Investigation of the peri-implanted bone tissue during the healing period after the insertion of intraosseal osseointegratable implants by means of single photon emission computer tomography [SPECT] with ^{99m}Tc -MDP.

2. Investigation of the bone density in the regions of implanting by means of CBCT. Comparison of the obtained results from the single photon emission computer tomography [SPECT] with ^{99m}Tc -MDP with the bone density before implantation.

3. Evaluation of the osseointegration on the third month after the insertion of intraosseal osseointegratable dental implants by means of magnetic resonance analysis. Comparison of the obtained results from SPECT with those from the MRI analysis.

Material and methods

Subject to the study are male and female patients over 18 years of age, in good general health status, e.g. without accompanying diseases, without a systemic medication intake, which can exert influence on the performance of the surgical manipulation for the insertion of the implants and interfere with the process of osseointegration. The investigated patients have their teeth extracted in the upper and/or lower jaw and there is a presence of sufficient bone volume to ensure the implant insertion without the need for performing bone augmentation.

The patients are selected according to strictly specified criteria for inclusion and exclusion for the study and have underwent the necessary preparation prior to the implantation.

The used methods of investigation are up-to-date and find application in the scientific research process during the period of healing of the intraosseal dental implants. This confirms Dr. Ivailo Hristov's strife to obtain results and draw conclusions which could facilitate the clinical practice and the approach in the treatment with dental implants.

In his work, the PhD student presents a specially developed software algorithm, by means of which to measure the mean values of bone density in a defined in advance bone volume of the cone beam computer tomography. The designed algorithm is unique of its kind in the world and ensures constancy in the measurements in different time periods, regions and patients, thus allowing for additional investigations and analyses. The method is fully clinically applicable and can be used in the everyday practice as an addition to the analysis prior to the implant treatment.

The statistical methods described allow for the detailed visualization of the tasks set.

The results obtained for the separate tasks confirm the profound analysis of the clinical material. In spite of the specificity of the processing Dr. Hristov presents it very clearly in tables and figures.

The PhD students presents his results and discussion on each of the tasks, comparing them to the already available results obtained by other authors who have performed similar investigations with various groups of patients.

The discussion is focused and competent. Dr. Hristov's ability is evident for analyzing the obtained results, on the basis of which he formulates 15 conclusions. These conclusions logically follow the aim and tasks set in the study.

The scarce publications and information in the literature indicate that his research is timely and it makes it possible to apply an adequate algorithm for implant treatment with a follow-up of the healing process.

The single photon emission computer tomography is a non-invasive, highly sensitive method ensuring not only anatomical picturing of the investigated area but also quantitative information associated with the physiological and dynamic changes occurring during the process of osseointegration.

One of the main challenges for the modern dental implantology is the development of treatment protocols allowing for shorter periods of treatment and faster rehabilitation of the toothless regions. This necessitates the development of new implant systems, testing of new materials and new implant surfaces. The increasing number of patients with risk factors necessitate the evaluation of the osseointegration process and its monitoring in time. To do this, investigations have to be performed together with the analysis and comparison of the results from the different methods. The combination of methods can cover a greater percentage of the factors influencing the osseointegration process. The greater the number of methods known and applied by the clinicians, the more critical they will be to their work. Owing to their non-invasiveness and specificity, the magnetic resonance analysis and the single photon emission computer tomography can be used in the assessment of all the variables in the course of treatment with dental implants.

Assessment of the contributions

The contributions are presented by Dr. Hristov accurately and correctly and are determined as contributions of affirmative nature and contributions of genuine nature for our country and the world. The most significant of them are the following:

1. For the first time, for the determination of the bone density of CBCT a software algorithm is developed to define the mean values of the Hounsfield units in bone volume specified in advance.

2. For the first time in Bulgaria, single photon emission computer tomography is applied with radiopharmaceutical ^{99m}Tc -MDP to evaluate the osteoblastic activity in the peri-implanted bone tissue during the healing period after the insertion of intraosseal osseointegratable dental implants.

3. For the first time in Bulgaria, the osteoblastic activity is compared with single photon emission computer tomography with radiopharmaceutical ^{99m}Tc -MDP according to the age and sex.

4. For the first time in Bulgaria, the relation is examined between bone density in the toothless regions of the jaw and the osteoblastic activity in these zones after implantation.

5. For the first time in Bulgaria, a comparative assessment is made between the values from the magnetic resonance analysis and the single photon emission computer tomography on the third month after the insertion of intraosseal osseointegratable dental implants.

Dr. Hristov has submitted 3 publications in scientific periodicals. He is the first author of all these publications. The publications look at various aspects of the obtained results and the literary reviews focusing on the application of single photon emission computer tomography with radiopharmaceutical ^{99m}Tc -MDP for the assessment of osteoblastic activity.

The dissertation summary covers 75 pages and fully reflects the dissertation thesis.

Conclusion

In conclusion, I would like to state my positive evaluation of the clinical and research activities underlying Dr. Ivailo Hristov's dissertation thesis and I will cast my confident and categorical "YES" vote. I propose to the honorable Scientific Jury to confer the educational and qualification degree "Philosophy Doctor" to Dr. Ivailo Georgiev Hristov within scientific specialty "Therapeutic dental medicine", professional division 7.2. "Dental medicine" in the field of higher education 7. "Healthcare and sports".

10.05.2022

Prof. Dr. Aneliya Klisarova, MD, PhD, DSc