"TITU MAIORESCU" UNIVERSITY BUCHAREST

FACULTY OF DENTAL MEDICINE

DOCTORAL SCHOOL

DOCTORAL THESIS

ABSTRACT

Titanium in Oral Implantology: An Integrative Mechanobiological Model and Patients' Perception

Scientific Supervisor:

Prof. Univ. Dr. FLORENTINA CORNELIA BÎCLEŞANU

PhD Candidate:

Mădălin Dorel ȚAP

BUCHAREST, 2026

CUPRINS

INTRODUCTION 7

CURRENT STATE OF KNOWLEDGE 11

CHAPTER 1. INTEGRATION OF TITANIUM AND TITANIUM ALLOYS IN ORAL IMPLANTOLOGY 12

1.1. THE IMPORTANCE OF USING TITANIUM AND TITANIUM ALLOYS IN ORAL IMPLANTOLOGY 12

1.2. THE EVOLUTION OF THE USE OF TITANIUM AND TITANIUM ALLOYS IN ORAL IMPLANTOLOGY 12

1.3. THE UTILITY AND BIOCOMPATIBILITY OF TITANIUM IN ORAL IMPLANTOLOGY 17

1.3.1. The utility of titanium in oral implantology 17

1.3.2. The biocompatibility of titanium in oral implantology 19

1.4. FACTORS AFFECTING THE OSSEOINTEGRATION PROCESS OF TITANIUM DENTAL IMPLANTS 21

CHAPTER 2. ANALYSIS OF THE CHARACTERISTICS OF TITANIUM IMPLANTS IN ORAL IMPLANTOLOGY 25

2.1. ADVANTAGES AND DISADVANTAGES OF USING TITANIUM AND TITANIUM ALLOYS IN DENTAL IMPLANTOLOGY 25

2.2. ANALYSIS OF THE STRENGTH AND SURFACE TREATMENT OF TITANIUM IMPLANTS 33

2.2.1. Surface treatment methods for titanium dental implants 33

2.2.2. Strength analysis of titanium dental implants – FEA Analysis 38

2.3. CHARACTERISTICS IDENTIFIED IN THE OSSEOINTEGRATION OF TITANIUM IMPLANTS 42

CHAPTER 3. ADVERSE EFFECTS THAT MAY OCCUR FOLLOWING THE USE OF TITANIUM AND TITANIUM ALLOYS IN ORAL IMPLANTOLOGY 46

3.1. ADVERSE EFFECTS OF TITANIUM USE IN ORAL IMPLANTOLOGY 46

3.1.1. Release of titanium particles into the body and the development of titanium hypersensitivity 47

3.2. ADVERSE EFFECTS THAT MAY OCCUR FOLLOWING THE USE OF DENTAL IMPLANTS MANUFACTURED FROM TITANIUM ALLOYS 49
ORIGINAL RESEARCH 54
CHAPTER 4. RESEARCH HYPOTHESES AND OBJECTIVES 55
4.1. RESEARCH OBJECTIVE 55
4.2. CENTRAL HYPOTHESIS 56
4.3. RESEARCH HYPOTHESES 56
4.4. GENERAL OBJECTIVE57
4.5. SPECIFIC OBJECTIVES 57
4.5.1. Patient perception objectives 57
4.5.2. Biomechanical objectives (FEA) 57
4.5.3. Analytical objectives (ICP-MS) 57
4.5.4. Cytological objectives 58
4.5.5. Correlation and statistical objectives 58
4.5.6. Clinical objectives 58
CHAPTER 5. INVESTIGATION OF PATIENTS' PERCEPTION OF TITANIUM DENTAL IMPLANTS AND THEIR ADVERSE EFFECTS ON THE HUMAN BODY 59
5.1. INTRODUCTION 59
5.2. AIM OF THE STUDY 59
5.3. STUDY OBJECTIVES 59
5.4. STUDY HYPOTHESES 60
5.5. MATERIALS AND METHODS62
5.5.1. Questionnaire design 63
5.5.2. Conceptual and operational definition of the research variables 64
5.5.3. Data collection 68
5.6. RESULTS 69
5.6.1. SEM analysis using WarpPLS 77
5.6.2. Hypothesis validation 78
5.6.3. Validation of the research model 79
5.7. DISCUSSION 80

5.8. CONCLUSIONS 83
CHAPTER 6. NUMERICAL ANALYSIS OF THE INFLUENCE OF CORROSION DEGRADATION ON A TITANIUM DENTAL IMPLANT 85
6.1. INTRODUCTION 85
6.2. NUMERICAL ANALYSIS – CONCEPTUAL ASPECTS 87
6.3. AIM OF THE STUDY 88
6.4. MATERIALS AND METHODS 88
6.4.1. Geometric modelling of the implanted structure 88
6.4.2. Mechanical properties of the materials 91
6.4.3. Finite element analysis parameters 92
6.4.4. Compression mechanical testing of the simulated implant–bone interface 94
6.4.5. Definition of the loading conditions applied to the resulting structure 95
6.5. RESULTS 95
6.5.1. Results of the mechanical tests 95
6.5.2. Results of the numerical simulation 97
6.6. DISCUSSION 106
6.7. CONCLUSIONS 111
CHAPTER 7. ASSESSMENT AND QUANTIFICATION OF TITANIUM PARTICLES AND IONS IN PERI-IMPLANT TISSUES BY EXFOLIATIVE CYTOLOGY AND ICP-MS ANALYSIS 115
7.1. INTRODUCTION 115
7.2. AIM OF THE STUDY 116
7.3. STUDY OBJECTIVES 116
7.3.1. General objective 116
7.3.2. Specific objectives 116
7.4. STUDY HYPOTHESES 116
7.4.1. Main hypothesis 116
7.4.2. Secondary hypotheses 117
7.5. MATERIALS AND METHODS 117
7.5.1. Sampling protocol 119
7.5.2. ICP-MS protocol (ICP-MS 8800 Triple Quad (Agilent Technologies))) 121

7.5.3. Statistical analysis 121
7.6. RESULTS 122
7.6.1. The demographic distribution of the study cohort included analysis of sex, age, implant location, implant type, implant age, and the main systemic and behavioural factors 122
7.6.2. Analysis of titanium concentration 126
7.6.3. Significance of the co-presence of other titanium-associated ions determined by ICP-MS spectrometry 128
7.6.4. Correlation analysis between clinical risk factors and titanium concentrations according to implant age 133
7.7. DISCUSSION 137
7.8. CONCLUSIONS 146
CHAPTER 8. FINAL CONCLUSIONS 147
CHAPTER 9. ORIGINAL CONTRIBUTIONS OF THE STUDY 150
BIBLIOGRAPHY 153
APPENDICES 183

Keywords: titanium, oral implantology, ICP-MS, FEA, exfoliative cytology, patients' perception;

SUMMARY

The doctoral thesis called "*Titanium in Oral Implantology: An Integrative Mechanobiological Model and Patients' Perception*" investigates the role of titanium in oral implantology from an integrative perspective. This work examined the biomechanical advantages of this material, as well as the adverse effects associated with the release of titanium ions and particles. The main objective of this thesis was to develop a mechanobiological model of titanium release into peri-implant tissues and to assess patients' perception of titanium dental implants.

With regard to the structure of the thesis, it should be noted that it was divided into nine chapters. The first three chapters presented the current state of knowledge, while the following six chapters comprised the original research. The first part of the doctoral thesis consisted of a critical review of the scientific literature, whereas the second part included three original research studies.

The first three chapters are intended to present the main theoretical concepts relating to the use of titanium in oral implantology. Accordingly, relevant information is provided regarding the evolution of the use of titanium and titanium alloys in this field of dentistry, as well as the principal advantages and disadvantages associated with the use of this material in dental implantology. Building upon the concepts analysed in the first part, the second section included a mechanobiological assessment of titanium release in peri-implant tissues, a finite element analysis (FEA), and, subsequently, an evaluation of the perception of patients with at least one titanium dental implant.

The second section of the thesis (original research) comprises four chapters: *"Research Hypotheses and Objectives*" and three research studies. "*Investigating Patients' Perception of Titanium Dental Implants and Their Adverse Effects on the Human Body*" is a quantitative study aimed at identifying how patients perceive titanium dental implants. Furthermore, it sought to determine the extent to which patients are aware of the potential adverse effects that may arise from the use of titanium dental implants. The quantitative research was conducted on a sample of 162 respondents. Data were collected using a questionnaire administered through an online platform.

The results showed that the main reasons why patients chose a titanium dental implant were its high success rate, strength and long-term durability, as well as the perception that these types of implants are safe for the human body. The analysis also revealed that a large proportion of the study

participants considered titanium dental implants to have a high success rate, enabling the restoration of masticatory function.

Furthermore, participants were of the opinion that these implants contribute to achieving satisfactory aesthetic outcomes. On the other hand, those who took part in the study considered these medical devices to be highly durable and capable of rapidly replacing the natural teeth they had lost. In addition to these perceived benefits, respondents stated that, when discussing titanium dental implants, the main risks that may arise should also be taken into account. Thus, they considered the most significant risks to be the occurrence of infections and peri-implantitis.

In addition to the univariate analysis performed, a conceptual model was also proposed and subsequently tested using WarpPLS 8.0 software. The results demonstrated that perceived benefits, anticipated problems, the level of risk awareness, and previous adverse experiences influence both the overall perception of titanium implants and the intention to undergo similar implant treatments in the future. Therefore, it can be stated that the analysis of the econometric model revealed the existence of significant relationships among the variables considered in the study. Furthermore, it was observed that the advantages of these medical devices have the capacity to generate a positive perception of them, while previous experiences and the level of risk awareness exert a substantial influence on the decision-making process. Overall, the results showed that both perceived benefits and associated risks are capable of influencing patients' decision-making processes, contributing to the formation of their perception of titanium dental implants and, at the same time, affecting their intention to use such implants in the future.

The chapter entitled "*Numerical Analysis of the Influence of Corrosion Degradation on a Titanium Dental Implant*" investigated the biomechanical behaviour of the dental implant–alveolar bone complex under conditions of progressive corrosion degradation by means of finite element analysis (FEA). From a methodological perspective, it should be noted that the aim of this research was to develop a three-dimensional model of the dental implant–alveolar bone complex, to which a finite element analysis was applied. The study presented the mechanical properties of the materials used and, at the same time, simulated different degrees of corrosion degradation in order to reproduce the structural changes that may occur over time within the implant. Both axial and oblique loading conditions were analysed.

The results of the mechanical tests and numerical simulations showed that corrosion degradation has the potential to significantly influence stress distribution. Furthermore, it affects

the functional behaviour of the implant system. The findings also highlighted the need for optimisation of implant design, appropriate selection of biomaterials, and the implementation of correct prosthetic protocols in order to maintain long-term stability. In addition, it was observed that the progression of corrosion leads to the development of local stress concentrations and significantly alters force transfer at the implant–bone interface.

Thus, it was demonstrated that, as material degradation progresses, the risk of implant mechanical failure and marginal bone resorption increases. This is due to the non-uniform distribution of stresses. Furthermore, it was observed that oblique loading generates higher stress values compared with axial loading. This aspect amplifies the effects of corrosion and facilitates the occurrence of the stress-shielding phenomenon. The results also showed that long-term biomechanical stability largely depends on the integrity of the implant material and the geometry of the implant.

The chapter entitled "*Assessment and Quantification of Titanium Particles and Ions in Peri-implant Tissues by Exfoliative Cytology and ICP-MS Analysis*" investigates the biochemical and cellular changes occurring in peri-implant tissues following the use of titanium dental implants. The study was conducted on a cohort of patients divided into distinct groups according to temporal criteria represented by the age of the dental implant. Accordingly, three groups were established: the recent implant group (7 days after implant placement), the 6-month implant group, and the long-term implant group, with implants in function for ≥ 1 year.

This classification made it possible to investigate the dynamics of titanium ion release. Furthermore, it enabled the identification of cytological changes associated with the different stages of peri-implant adaptation. The study also included a control group. This consisted of individuals who did not have a titanium dental implant at the time the research was conducted.

With regard to the sampling procedure, it should be noted that exfoliative cytology was used. Elemental analysis was performed by inductively coupled plasma mass spectrometry (ICP-MS). The results obtained from this study demonstrated that tissue titanium levels varied according to the age of the dental implants. This finding illustrated the pattern of titanium release over time. ICP-MS analysis also revealed the presence and variation of several ions associated with titanium. These ions originated either from the composition of the implants or from degradation and tribocorrosion processes occurring at the implant–tissue interface. In view of the aspects mentioned above, it should be noted that comparing titanium concentrations with those of the other detected

ions made it possible to identify patterns of co-occurrence and potential common release mechanisms. All these findings highlighted the existence of complex electrochemical degradation processes and local biological adaptation mechanisms.

Furthermore, the correlation analysis revealed the existence of relationships between tissue titanium concentrations and a number of patients' clinical and behavioural factors. Thus, it was observed that variations in titanium levels are influenced not only by the age of the dental implant but also by the patient's local and systemic characteristics. These findings demonstrated the existence of a complex interaction between peri-implant biological processes, mechanical loading, and the individual conditions of each patient. In view of these aspects, it should be noted that continuous monitoring of titanium concentrations may be considered highly important in the assessment of peri-implant stability. Furthermore, it also plays an important role in the early identification of factors that may favour the development of biological complications. Overall, the results obtained support the hypothesis that the release of titanium and associated ions is influenced both by biomechanical loading and by the characteristics of the peri-implant microenvironment.

The "*Final Conclusions*" highlighted the main findings and key implications of the thesis. It was observed that, although titanium and titanium alloys are currently regarded as some of the most widely used materials for the manufacture of dental implants, they should be investigated from a much broader and more comprehensive perspective. Such an approach should address not only the benefits offered by these materials but also the main risks that may arise from their use. The clinical studies conducted within the thesis demonstrated the presence of titanium particles and ions in peri-implant tissues. Furthermore, it was observed that their concentration varied according to the age of the dental implant.

In the final chapter of the thesis, entitled "*Original Contributions of the Study*", the main original and novel aspects of the research were presented The originality of the work lies in the integration of different analytical methods. In view of the above, it should be noted that this thesis contributes added value both to the scientific literature and to clinical practice. It provides new insights into the biological behaviour of titanium in oral implantology and, at the same time, proposes future research directions aimed at optimising the materials used in dental implantology.