M U N I

UPDATE 18 MARCH 2021

COMMENTARY TO HABILITATION THESIS[1]

Title: Titanium beta alloys in dental implantology. Material properties, biocompatibility and osseointegration

Current state of knowledge

The presented habilitation thesis deals with titanium and titanium alloys in relation to their application in dentistry. The theoretical part of the thesis presents a summary of current knowledge about material properties, depending on their chemical composition and manufacturing technique. Attention is also paid to the biocompatibility of these alloys Special attention is given to the effects of alloying elements (Ta, Fe, Nb, V, Mo) on the material properties of titanium alloys and surface treatment methods to facilitate osseointegration. Factors influencing the osseointegration of titanium and its alloys are presented and described, especially the process of TiO_2 formation on the alloy surface and coating of the surface with materials to promote osseointegration. Attention is also paid to current trends in the research of titanium and titanium alloys for future use in dental implantology and clinical trials.

Objectives of the work

The experimental part of the work summarizes the long-term research of the above-specified topics carried out in the period of 2005-2011 within the Stomatological Center of the Medical Faculty of the Masaryk University and in the following years within the framework of partial projects. The aim of the research work was to characterize the properties of titanium alloys with addition of niobium and tantalum (Ti-38Nb, Ti-35Nb-6Ta and Ti-33.5Nb-5.7Ta) in terms of material properties, ion release from the alloy, corrosivity and biocompatibility evaluated by biotests. The aim was to quantify the influence of alloying elements of titanium β alloys on their cytotoxicity. Another aim of the work was to test the growth rate of osteoblasts and osteoclasts on the surface of hydroxyapatite-coated alloy using cell adherence and proliferation tests, and specific markers (amount of DNA and alkaline phosphatase activity). Last but not least, the aim was to apply mathematical modeling procedures to calculate stress distribution in dental implants of various types, in the implant-bone tissue system and in the jaw.

Methods

The following methods and procedures were used for the experimental and clinical part of the habilitation thesis: biocompatibility tests consisting of cytotoxicity tests, cell adherence tests, and quantification of osteoblast growth. Simulated body fluid and determination of released ions was done by X-ray photoelectron spectroscopy and used to quantify the corrosivity of titanium alloys. The adsorption of fibrinogen and deoxyoligonucleotides was monitored using a laser diffraction sensor. Cell adherence and proliferation were monitored by DAPI staining and microscopy. *In vivo* implant osseointegration assays (done on Ti38-Nb6-Ta alloy) were performed on minipigs using the relative percentage of bone-to-implant contact and implant stability (ISQ). Analysis of the surface microstructure of titanium alloys was performed by microfiling

[1] The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

using digital 3-D microscopy methods. The ANSYS version 3.5 software environment and the ADPL (Ansys Parameter Design Language) programming tool were used to model stresses in implants of various types, stress distribution in the implant-bone system and to model periodontal properties.

Results

The main results obtained using the methods specified above, which are the subject of published professional work, can be summarized as follows:

- Tests of the cytocompatibility of titanium alloys and alloying elements have shown that the suitability of ialloying elements decreases in the order of Ta Ni Va Mo.
- In the experiment using simulated body fluids to assess the corrosivity of the Ti-Nb-Ta alloy, low corrosivity was demonstrated and stinaTi-33.5NI-5.7Ta was characterized as biocompatible and suitable for the production of dental implants.
- Tests of cell adherence to the surface of titanium alloys and various alloying elements (Ta, Fe, Nb, V, Mo) have shown that Fe and V ions reduce the rate of adherence and the surface coverage of the tested material.
- Tests have shown that the surface treatment method significantly affects the growth of human osteoblasts on the Ti surface. The growth of osteoblasts was supported on the polished and etched surface compared to only the polished surface. Fibrinogen adsorption was promoted by surface treatment: titanium-enriched hydrocarbon coatings.
- The microroughness of the material positively influences the adsorption of deoxynucleotides on the titanium surface. A suitable micro- and nano-structure can be monitored using a diffractive optical sensor.
- An *in vitro* study demonstrated the suitability of coating the titanium surface with hydroxyapatite (sputtered HA) by evaluating cell adherence, density and growth (stromal cells of laboratory rats), selected markers (amount of DNA and alkaline phosphatase).
- Tests of VP dental implants performed *in vivo* in the tibia of minipigs (in collaboration with Tokyo Medical and Dental University) showed very good osseointegration and stability in bone (ISQ - implant stability qoutient).
- The micro- and nano-structure of the surface is important for the biointegration of the dental implant. Using AFM (Atomic force Microscopy) and 3-D digital microscopy techniques, the suitability of the surface structure created after the end of the technological phase, i.e. after individual types of surface treatment, can be effectively checked.
- Mathematical modeling in the ANSYS software environment can be used to determine deformation analysis of parts of dental implants (blade, cylindrical, disc implants are presented in the habilitation thesis), which show critically high stress values after insertion into bone tissue. Thus, potential fractures of dental implants can be indicated
- Mathematical modeling of the implant-bone system and simulation of variously large masticatory forces acting on the implant can be used to simulate and

predict the occurrence of critical stress in the periodontium and surrounding bone. These sites pose arisk of potential bone resorption.

The author's share in the preparation of published professional publications excerpted in the WOS database was in the range of 10-40% for publications with foreign co-authors. In the case of publications with national co-authors the share achieved 20-70%.

Conclusion

Based on the results presented in the habilitation thesis, it can be concluded that most titanium alloys are fully biocompatible or biotolerant. The issue of titanium and its alloys is developing dynamically in the field of medical research and clinical practice and, thanks to the rapid development of technologies, is promising for a wide application of these materials in dentistry.
text of the commentary]

[1] Bartáková, S., Málek, J., Prachár, P.: The Effect of Oxygen Addition on Microstructure and Mechanical Properties of Various Beta-Titanium Alloys. *Journal of Metals (JOM)*: 2019, 1-8. DOI: 10.1007/s11837-019-03879-w (IF: 2.305, METALLURGY & METALLURGICAL ENGINEERING Q1)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	60%	60%	60%

[2] Bartáková,S., Prachár,P., Dvořák,I., Hrubý, V.,Vaněk, J., Pospíchal E., Svoboda,E., Martikan,H.,Konečná, H., Sedlák, I.): Mechanical properties and microstructure of Ti-35.5Nb-5.7Ta beta alloy. *Bratislavské lékarské listy*, Bratislava: Univerzita Komenského v Bratislave, 2015, 116, 2, 88-92. ISSN 0006-9248. DOI: 10.4149/BLL_2015_016 (IF: 0.454, MEDICINE, RESEARCH & EXPERIMENTAL Q3)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	50%	80%	70%

[3] Prachár, P, **Bartáková,S**., Březina,V., Cvrček, L.,Vaněk, J.: Cytocompatibility of implants coated with titanium nitride and zirconium nitride. *Bratislavské lekárske listy*, Bratislava, 2015, 116/2015, 3, 154-156. ISSN 0006-9248. DOI: 10.4149/BLL_2015_031 (IF: 0.454, MEDICINE, RESEARCH & EXPERIMENTAL Q3) **Equal first authorship of P. Prachár and S. Bartáková**

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	50%	50%	50%

[4] Málek, J., Hnilica, F,**Bartáková, S**., Míka, P., Veselý, J.: The effect of different forms of oxygen on properties of Beta titanium alloys. *Acta Polytechnica*, 2018, 58: 179-183. DOI: 10.14311/AP.2018.58.0179, (indexed in WOS in All Databases, IF not yet given)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	50%	45%	65%

[5] Tsutsumi, Y., **Bartáková, S**., Prachár, P., Yalatu, S., Migita, S., Doi, H., Nomura, N., Hanawa, T.: Long-Term Corrosion Behavior of Biocompatible β-Type Ti Alloy in Simulated Body Fluid. *Journal of The Electrochemical Society*, 2012, 159: 435-440, ISSN: 0013-4651. DOI: 10.1149/2.045210jes (IF: 2.588 MATERIALS SCIENCE, COATINGS & FILMS Q1)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25%	55%	55%	100%

[6] Prachár, P., **Bartáková, S**., Vaněk, J.: The titanium PV I endosteal implant from beta – titanium alloy Ti 38Nb 6Ta. *Biomedical Papers of the Faculty of Medicine of Palacký University*, 2015, 159(3):503-7. ISSN 1213-8118. DOI: 10.5507/bp.2014.011 (IF: 0,924, MEDICINE, RESEARCH & EXPERIMENTAL Q4)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30%	35%	45%	45%

[7] Málek J., Hnilica F., Smola B., **Bartáková S**., Vaněk J. : The influence of chemical composition and thermo-mechanical treatment on Ti-Nb-Ta-Zr alloys. *Materials and Design*, 2012, 35: 731-740. DOI: 10.1016/j.matdes.2011.10.030 (IF: 2.913, MATERIALS SCIENCE, MULTIDISCIPLINARY Q1)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	50%	50%	50%

[8] Málek, J., Hnilica, F., Veselý, J., Smola, B., **Bartáková, S.,** Vaněk, J. : Microstructure and mechanical properties of Ti-35Nb-6Ta alloy after thermomechanical treatment. *Materials Characterization*, 2012, 66: 75-82. ISSN1044-5803. DOI: 10.1016/j.matchar.2012.02.012 (IF: 1.88 MATERIALS SCIENCE, CHARACTERIZATION & TESTING Q1)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	60%	40%	50%

[9] Hao, J., Kuroda, S., Ohya, K., **Bartáková, S.,** Aoki, H., Kasugai, S.: Enhanced osteoblast and osteoclast responses to a thin film sputtered hydroxyapatite coating. Journal of Materials Science: Materials in Medicine. 2011, 22:1489-99. DOI: 10.1007/s10856-011-4329-0 (IF: 3.316 ENGINEERING / MATERIALS SCIENCE, BIOMATERIALS Q2/Q3)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30%	40%	60%	80%

[10] Borák, L., Florian, Z., **Bartáková, S.,** Prachár, P., Murakami, N., Ona, M., Igarashi, Y., Wakabayashi, N.: Bilinear elastic property of the periodontal ligament for simulation using a finite element mandible model. Dental Materials Journal, 2011, 30:448-454. ISSN: 0287-4547. DOI: 10.4012/dmj.2010-170 (IF: 1.137 DENTISTRY, ORAL SURGERY & MEDICINE Q3)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	60%	30%	60%

[11] Strecha, J., Jurkovic, R., Siebert,T., Prachar, P., **Bartakova,S.** : Fixed Bicortical Screw and Blade Implants as a Non-Standard Solution to an Edentulous (Toothless) Mandible. *International Journal of Oral Science*, 2, 2010, 105-110, ISSN 1674-2818. 2010. DOI: 10.4248/IJOS10030 (IF: 0.815 DENTISTRY, ORAL SURGERY & MEDICINE Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	30%	30%	30%

[12] Silvennoinen, R., Hasoň S., Vetterl, V., Penttinen, N., Silvennoinen, M., Myller, K., Černochová, P., **Bartáková, S.,** Prachár, P., Cvrček, L.: Diffractive-optics-based sensor as a tool for detection of biocompatibility of titanium and titanium-doped hydrocarbon samples. *Applied Optics*. 2010, 49:5583-5591, ISSN: 0003-6935 DOI: 10.4248/IJOS10030 (IF: 0.815 DENTISTRY, ORAL SURGERY & MEDICINE Q1)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	10%	10%	10%

[13] Manogue, M., Kelly, M., **Bartáková, S.,** Brown, G., Catalanotto, F., Choo-Soo, T., Delap, E., Godoroja, P., Morio, I., Rotgans, J., Saag, M. : Evolving methods of assessment. *European Journal of Dental Education*, 2002, 6 (Suppl. 3): 53-66. – EJDE is listed in WOS since 2009.DOI: 10.1034/j.1600-0579.6.s3.8.x (IF: v daném roce publikace nebyl, IF byl časopisu přidělen v roce 2009 IF:1,024 DENTISTRY, ORAL SURGERY & MEDICINE Q3)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60%	40%	70%	80%

[14] Málek, J., Hnilica, F., **Bartáková, S.,** Veselý, J.: The effect of Solution Treatment Temperature on Plastic Deformation and Fracture Mechanisms of Beta - Titanium Alloy. *Solid State Phenomena*, 2017: 218-223. ISSN 1012-0394. DOI: 10.4028/www.scientific.net/SSP.270218.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30%	30%	60%	60%

[15] Marcián, P., Borák, L., Florián, Z., **Bartáková, S.** Konečný, O., Navrátil, P. : Biomechanical study of the bone tissue with dental implants interaction. *Applied*

and Computational Mechanics, 2012, 2011, 2, 173-186. ISSN: 1802- 680X.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	30%	40%	40%

[16] Bartáková S., Prachár P., Kudrman J., Březina V. , Podhorná B. , Černochová P. , Vaněk J. , Strecha J. : New titanium β-slloys for dental implantology and their laboratory-based assays of biocompatibility. *Scripta Medica*, 2009, 82: 76-82

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	90%	90%	90%

[17] Bartáková, S., Suchánek, J., Mičulka, J., Vaněk, J: Computer simulation of bony tissue response to a partial removable denture fitted to a lower jaw. *Scripta Medica* 2003, 76, 21-28.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60%	70%	90%	90%

[18] Bartáková, S., Prachár,P., Podhorná, B., Březina, V., Vaněk, J., Strecha, J., Hnilica, F.: Titan a titanové beta slitiny: současné trendy ve výzkumu a vývoji pro aplikaci v dentální implantologii. *Progresdent*, 2009, 15: 36-41.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	60%	90%	30%

[19] Bartáková, S., Prachár, P., Vaněk J.: Klasifikace defektů chrupu. *StomaTeam*, 2/2008, 8, s. 18-20, ISSN 1214-147X.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
80%	80%	90%	80%

[20] Bartáková, S., Prachár, P., Vaněk, J.: Klasifikace Defektů chrupu II*. StomaTeam*, 3/2008, 8, s. 24-26, ISSN 1214-147X.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
80%	80%	90%	80%

[21] Bartáková, S., Prachár, P., Cvrček, L., Březina, V., Vaněk, J.: Vyhodnocení chemické stability povlakované vrstvy nitridu zirkonia na základní konstrukci z chromkobaltové slitiny. *Praktické zubní lékařství*, 55, 2007, 4, 63-66.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30%	30%	90%	30%

[22] Bartáková, S., Vaněk, J. (2004): Index CPITN u fixních protetických náhrad z Wironu a drahokovu Aufixu. *Česká Stomatologie*. 2004, 104, 135-139, ISSN 1210-7891

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
90%	100%	100%	100%

[23] Prachár, P., **Bartáková, S**., Kasugai, S., Martikáň, A., Martikáň, T., Vaněk, J. (2011): Povlakování HA u modifikace implantátu PV I, *Stomatológ,* 2011, Bratislava, 21, 1, 48-54, ISSN 1335-0005.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	50%	50%	50%

[24] Borák, L., Marcián, P., Florián, Z., **Bartáková, S.** (2010): Biomechanical Study of Disk Implants, Part I. *Engineering Mechanics,* 2010, roč. 17, č. 1, s. 49-60. ISSN: 1802- 1484.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	60%	20%	40%

[25] Bartáková, S., Prachár, P., Kudrman, J., Podhorná,B., Březina,V., a Strecha,J. (2009): Binární titan-niobové slitiny a jejich biokompatibilita. *Stomatológ*, Bratislava: Slovenská komora zubných lekárov, 2009, IX, 1, 39-42, ISSN 1335-0005. 2009.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	60%	100%	20%

[26] Bartáková, S., Prachár,P., Strecha, J.,Podhorná, B., Březina , V., Vaněk, J. Titanové slitiny s příměsí železa:Analýza materiálových vlastností, biokompatibility a vhodnosti pro aplikaci v dentální implantologii. *Stomatológ*, Bratislava: Slovenská komora zubných lekárov, 2009, 19, 2, 19-24,ISSN 1335-0005.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30%	30%	100%	30%

[27] Silvennoinen, R., Penttinen, N., Silvennoinen, M., Strecha, J., Hasoň. S., Vetterl, V., **Bartáková, S**., Prachár, P., Vaněk, J., Březina, V.: Optical Detection of Protein Adsorption

on Doped Titanium Surface. In *Biomaterials Science and Engineering*. Croatia: InTech open beta, 2011, 173-190, ISBN 978-953-307-609-6.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30%	30%	40%	30%

[28] MASARYKOVA UNIVERZITA, BRNO, ČR A ING. ANTON MARTIKÁŇ, DOLNÁ MARIKOVÁ, SK A FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ, ČR A UJP PRAHA A.S., PRAHA ČR, 2012. Dentální implantát I. Původci: Patrik PRACHÁR, Sonia BARTÁKOVÁ, Juraj STRECHA, Jiří VANĚK, František HNILICA, Vítězslav BŘEZINA a Anton MARTIKÁŇ. Česká republika. PVZ 2011-38887 / 35431/ 24-03. 28.11.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	40%	40%	40%

[29] MASARYKOVA UNIVERZITA, BRNO, ČR A ING. ANTON MARTIKÁŇ, DOLNÁ MARIKOVÁ, SK A FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ, ČR A UJP PRAHA A.S., PRAHA ČR, 2012. Dentální implantát II. Původci: Patrik PRACHÁR, Sonia BARTÁKOVÁ, Juraj STRECHA, Jiří VANĚK, František HNILICA, Vítězslav BŘEZINA a Anton MARTIKÁŇ. Česká republika. PVZ 2011-38888 / 35432/ 24-03. 28.11.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	40%	40%	40%

[30] MASARYKOVA UNIVERZITA, BRNO, ČR A ING. ANTON MARTIKÁŇ, DOLNÁ MARIKOVÁ, SK A FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ, ČR A UJP PRAHA A.S., PRAHA ČR, 2012. Dentální implantát III. Původci: Patrik PRACHÁR, Sonia BARTÁKOVÁ, Juraj STRECHA, Jiří VANĚK, František HNILICA, Vítězslav BŘEZINA a Anton MARTIKÁŇ. Česká republika. PVZ 2011-38889 / 35433/ 24-03. 28.11.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	40%	40%	40%

[31] MASARYKOVA UNIVERZITA, BRNO, ČR A ING. ANTON MARTIKÁŇ, DOLNÁ MARIKOVÁ, SK A FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ, ČR A UJP PRAHA A.S., PRAHA ČR, 2012. Dentální implantát IV. Původci: Patrik PRACHÁR, Sonia BARTÁKOVÁ, Juraj STRECHA, Jiří VANĚK, František HNILICA, Vítězslav BŘEZINA a Anton MARTIKÁŇ. Česká republika. PVZ 2011-38890 / 35434/ 24-03. 28.11.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	40%	40%	40%

[32] MASARYKOVA UNIVERZITA, BRNO, ČR A ING. ANTON MARTIKÁŇ, DOLNÁ MARIKOVÁ, SK A FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ, ČR A UJP PRAHA A.S., PRAHA ČR, 2012. Dentální implantát V. Původci: Patrik PRACHÁR, Sonia BARTÁKOVÁ, Juraj STRECHA, Jiří VANĚK, František HNILICA, Vítězslav BŘEZINA a Anton MARTIKÁŇ. Česká republika. PVZ 2011-38891 / 35435/ 24-03. 28.11.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	40%	40%	40%

[33] Sadr, A., **Bartáková, S**., Prachár, P. et al.: Adhesion of flowable composite in class 1 cavities. Combination of SS-OCT Imaging and Microtensile Bond Strength. The 4th International Conference on Adhesive Dentistry (IAD), Seoul, South Korea, 2011, Abstract no. OP07. **Winner Poster 2011**

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50%	50%	60%	40%

[34] BARTÁKOVÁ S. Protetická stomatologie. In: VANĚK, J. (ed.), A. FASSMANN, L. IZAKOVIČOVÁ HOLLÁ, A. VAŠKŮ, M. MACHÁLKA, L. ROUBALÍKOVÁ, L. PROCHÁZKOVÁ, P. PRACHÁR, S. BARTÁKOVÁ, O. BULIK, P. ČERNOCHOVÁ, H. POSKEROVÁ, P. AUGUSTIN, J. ŠOUKALOVÁ, R. GAILLYOVÁ. *Stomatologie pro studující všeobecného lékařství: dodatek skript*. 1. vyd. Brno: Masarykova univerzita, 2010. s. 21 – 26. ISBN 978-80-210-5121-8.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
100%	100%	100%	100%