## Reg. No: 2023/51/D/ST11/02078; Principal Investigator: dr in . Michał Bartma ski

Metals and their alloys, mainly titanium, remain the most commonly used material group for long-term implants including hip or knee endoprostheses or dental implants. The titanium alloys with a  $\beta$ -type structure have closer mechanical properties to the bone than the titanium alloys with aluminum and vanadium which are currently most often used in implantology and these are worth attention.

Unfortunately, despite efforts, the problem of numerous reimplantation still remains unsolved, and the reasons for revision procedures are mainly implant loosening, bacterial infections and dislocation of endoprostheses. Implant loosening can be caused by a huge difference between the high mechanical properties of the implant and the relatively low mechanical properties of the bone, which can lead to the occurrence of the shielding effect, the symptom which is a reduction in bone density due to inappropriate loading and disruption of bone remodeling. Therefore current research aims to develop new titanium alloys with lowered mechanical properties, including alloys with the addition of zirconium, niobium and tantalum, which are stabilizers of the  $\beta$ -phase responsible for the reduction of mechanical properties, including mainly Young's modulus. Implant loosening can also occur due to too slow integration of damaged bone tissue into the implant.

The solution to the problem of bacterial infections seems to be the modification of implant surfaces using metal nanoparticles with proven antibacterial properties, e.g. silver, gold, copper or zinc. However, it has been proven in scientific studies that excessive concentrations of these elements can have a cytotoxic effect on living cells. Therefore it remains important, to maintain the right balance between obtaining antibacterial properties of the modification and maintaining its lack of cytotoxicity. Another problem is the release of the antibacterial substance from the surface of the implant only in the first period after implantation, which does not provide a long-term antibacterial cover. The challenge of modern science, therefore, remains the development of such a hybrid surface modification of advanced titanium alloys, which immediately after implantation would provide adequate terms for primary stabilization by reducing inflammation occurring due to bone damage, while maintaining bioactivity and providing long-term antibacterial protection without cytotoxic effect.

The problems presented motivated the development of the proposed project. The project provides for the fabrication on a  $\beta$ -type titanium alloy (Ti35Nb7Zr5Ta) with similar mechanical properties to bone, at an initial stage, with variable parameters of micro-arc oxidation of coatings with zinc and calcium ions, and then deposition, on such a modified surface, by the electrophoretic method of coatings based on chitosan with the addition of nanohydroxyapatite and zinc nanoparticles. Appropriate parameters of micro-arc oxidation will allow the incorporation of a certain amount of zinc ions inside the ceramic porous matrix of the coating, which will provide long-term antimicrobial properties and increase the adhesion of the chitosan-based coating deposits. The chitosan-based coating with the addition of nanohydroxyapatite and zinc nanoparticles will provide sufficient bioactivity and, due to the instability of chitosan only at reduced pH, will provide antibacterial shielding only in the presence of inflammation and bacterial infection. In the final stage, the hybrid modification thus produced will be functionalized with platelet-rich plasma, ensuring faster healing of damaged bone and enhancing osteoblast proliferation.

The obtained modifications will be a subject to full characterization including studies of structure (XRD), morphology and chemical composition (SEM+EDS, XPS and TEM), surface topography (AFM), nanomechanical properties and adhesion using nanoindentation technique and nanoscratch test (including insitu studies in SEM), corrosion resistance in a solution simulating human body fluids (OCP, EIS), degradation tests and ion release rate (MP-AES), wettability and surface energy testing, microbiological response (against Gram+, Gram- bacteria's and fungi). Biological tests will also be performed to determine the effect of the modification on the *in vitro* response against human osteoblasts and bone marrow-derived stem cells including cell viability tests, determination of alkaline phosphatase enzyme activity and cell mineralization, determination of energy potential and oxidoreductive potential, determination of intracellular calcium and zinc. The impact of the project's results in the development of scientific disciplines such as materials engineering and biomedical engineering is indisputable. In addition, the project about the interactions of material and biological factors will undoubtedly be useful in further basic research and subsequent considerations will have a significant impact on the population, because they will allow in the future to design a new class of long-term implants with high bioactivity and long-term antimicrobial cover to use in orthopedics or dentistry.