Antimicrobial passive coatings for titanium dental implants

TÉCNICO LISBOA

DBE DEPARTAMENTO DE BIOENGENHARIA TÉCNICO LISBOA

Miguel Mendes de Oliveira[1], Ana Paula Serro[2], Rogério Colaço[3]

1- PhD candidate in Bioengineering: Cell Therapies and Regenerative Medicine. miguel.oliveira@campus.ul.pt
2 - Principal Researcher at CiiEM.
3 - Full Professor in the Mechanical Engineering Department of IST.

Introduction & Objective

Over the last decades, oral rehabilitation with dental implants became a routine procedure. Peri-implantitis, caused by bacterial infection, is a common associated complication, which often causes implant failure. Nowadays, it is considered the biggest challenge in dental medicine, due to its high and growing prevalence[1,2]. Although resective and regenerative therapies have been put forward to solve this problem, until now, no particular treatment protocol has revealed effective[3-5].

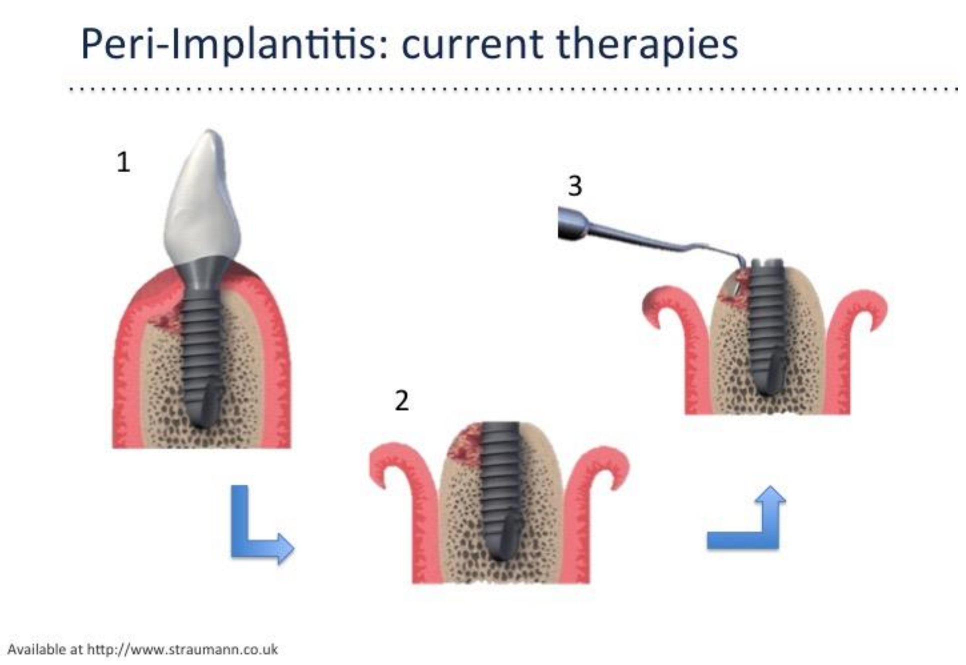


Figure 1. Currently, the management of peri-implantitis is focused on infection and bacterial controls, through surface decontamination.

To reduce the infection rates, several approaches have been attempted, including the development of antimicrobial coatings on implants. Active coatings, designed to release antimicrobial agents after implantation, may lead to high local toxicity and reduced long-term activity. Thus, recent research has focused on passive coatings that do not release antimicrobial agents but inhibit microbial adherence and/or kill the pathogens by contact[2,6]. Covalent binding of the antimicrobial agents has advantages over the non-covalent, namely a higher adhesion and a long-lasting antibacterial activity[5]. To the best of our knowledge, there are still no studies that allow understanding the effect of surgical placement of dental implants on the covalently bonded coatings, or any systematic comparison between systems of this type in terms of safety, efficacy and tribological behaviour.

The main objective of this project is to develop and optimize protocols to produce titanium dental implants with antimicrobial surface properties, through covalent binding of different antimicrobial agents to the implants surface.

Institutions

The project is framed in a call of the European Union funded network MERA.NET, that involves several research groups from academic institutions of Portugal, Brazil and Italy, with complementary skills in areas such as biomedical and materials engineering, medicinal chemistry, pharmacy and (micro)biology, that will work in straight cooperation with an industrial partner from Switzerland, Straumann, leader in solutions for implant dentistry.

UNIMORE UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

TÉCNICO LISBOA

FACULDADE DE MEDICINA VETERINÁRIA

FACULDADE DE CIÊNCIAS FARMACÊUTICAS

straumann

INSTITUTO SUPERIOR DE CIÊNCIAS DA SAÚDE EGAS MONIZ

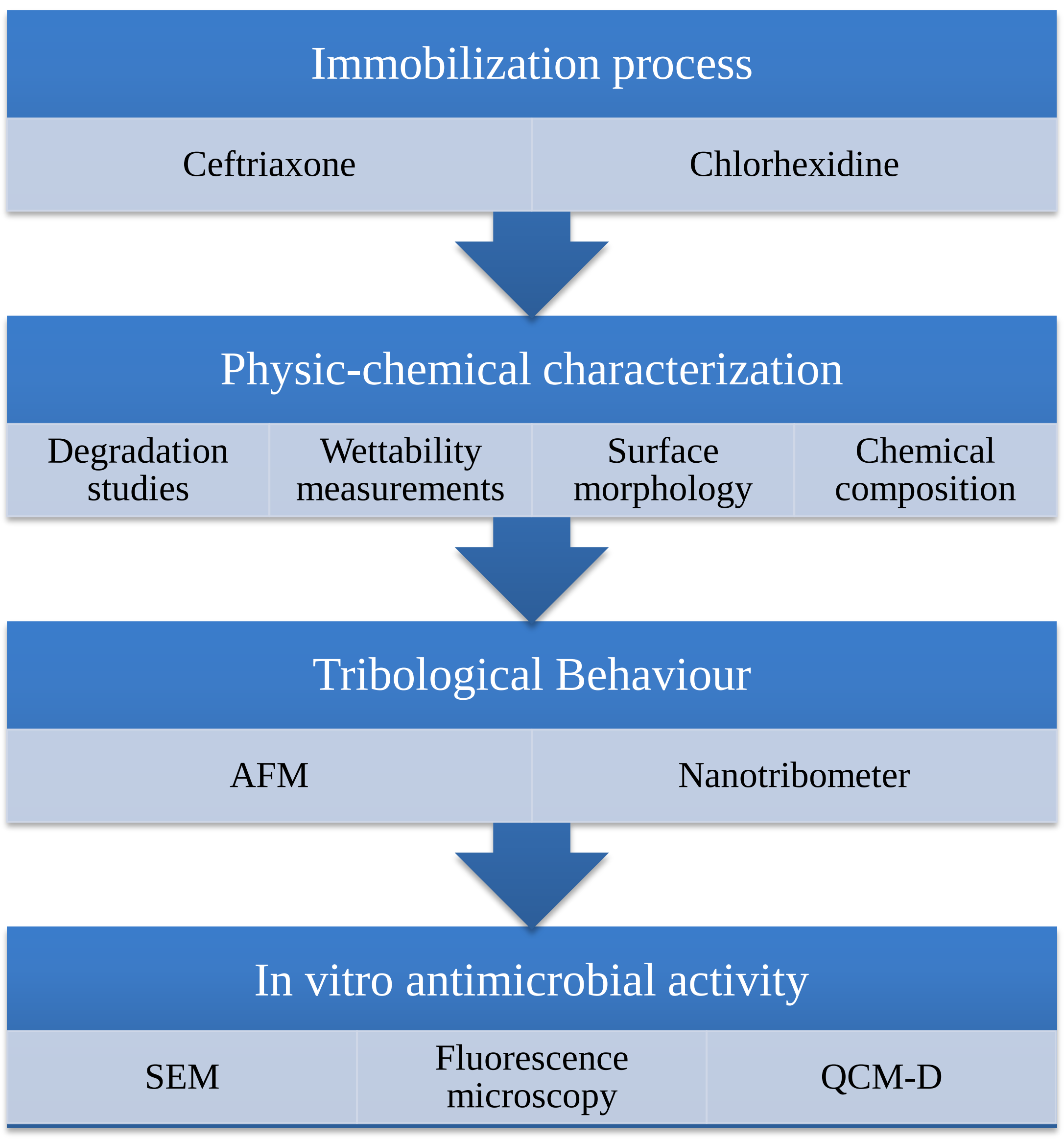
Research Plan

In the present work we propose a new improved solution to deal with per-implantits: smart dental implants coated with antimicrobial agents to act prophylactically. The idea is to bound irreversibly to the implants surfaces, through covalent bonds, certain drugs, carefully chosen to minimize the bacterial resistance, that are effective to prevent the bacterial contamination of the implanted devices. This requires a multidisciplinary approach to characterize the interaction between the implant material and the biological host tissues. In particular, aspects such as the biofilm inhibition potential, biodegradation and wear resistance of the coating, cytotoxicity and possible impact on the osteointegration process will be extensively studied. It is aim of this project to bring advance material-based technologies closer to the market by improving already existing medical devices.

To achieve this goal our work plan will comprehend 4 consecutive tasks:

1. **Immobilization** of antiseptics and/or antibiotics that will be carefully chosen, considering the molecules most used in clinical practice and less prone to induce drug resistance;
2. Relevant **physic-chemical properties** of the coated surfaces, such as wettability, morphology/topography, microhardness, stability, and others will be evaluated.
3. **Tribological studies** will be done at macro and micro/nano levels to investigate the effect of surgical implantation on the coatings wear resistance;
4. The **antimicrobial behavior** of the coatings will be investigated through standard test.

Project Methodology



Innovation and Originality

- Unmet need: Although the concept of antimicrobial coatings is welcomed both by clinicians and industry, which recognize the great advantages of this type of devices, this solution is still not commercially available;

- Applicability of the concept: The simplicity of the drugs immobilization method(s) proposed in this project shall lead to an easy integration in the current manufacturing processes. Furthermore, the concept can be extended to several other applications (e.g. orthopaedic, maxillofacial surgery).

- Antimicrobial resistance: In this work there is a concern of choosing carefully the antiseptics and/or antibiotics that will be used, to minimize antimicrobial resistance.

- Tribological characterization: For the first time, tribological behaviour of the functionalized surfaces will be evaluated through in vitro studies, to predict the wear resistance of the coatings upon implantation.

- Systematic study: A detailed characterization, which involves not only the determination of the physico-chemical properties, but also microbiological and tribological studies will be carried out to optimize the devices and will precede in vivo tests with animals. Such complete approach was never done before.

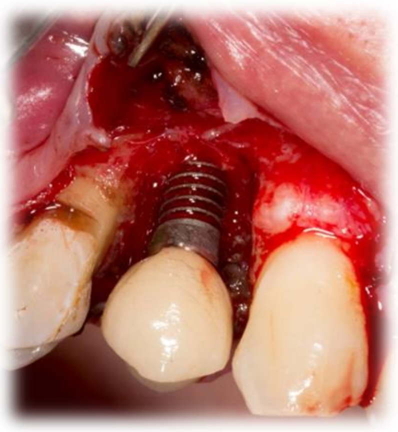
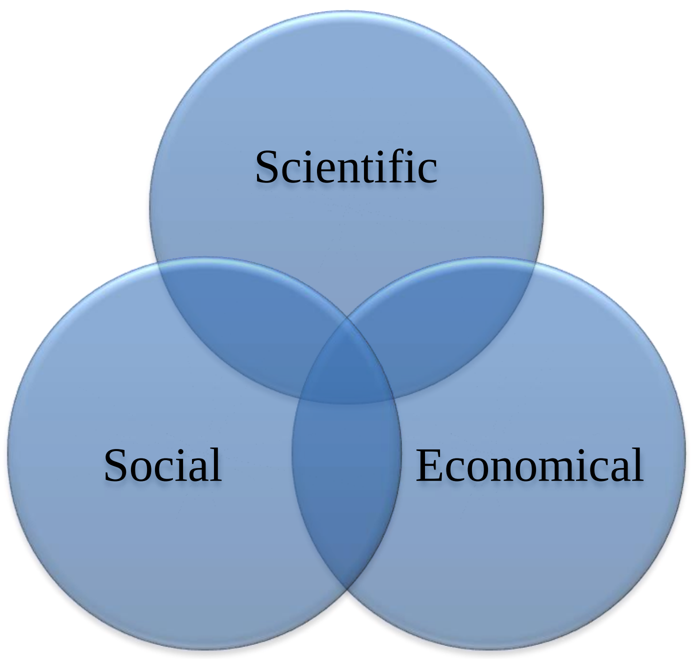


Figure 2. Unmet need. Peri-implantitis phenotype: bone loss around the implant. Courtesy of Miguel de Melo Costa DMD.

Impact



This project will be an optimal starting point to develop dental implants with antimicrobial surfaces and shall have impact at different levels, namely:

Social: The referred implants constitute a new solution for efficient and biological safe prevention of biofilm formation and they are expected to considerably improve people's quality of life and well-being, resulting in savings to patients and health care systems.

Scientific: New relevant scientific insights will be generated, which will allow to understand the complexity of functionalized dental implant interfaces and the biofundamentals of its action, going far beyond the current state of the art.

Economic: Given the inexistence in the market of this type of dental implants, their development is regarded with particular interest by dental implant manufacturers that look at it as a new opportunity of business.

References

1. Davidson H, Poon M, et al. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2014;103(7):1381- 1389.
2. Gerits E, Kucharíková S, et al. Journal of Orthopaedic Research. 2016. doi: 10.1002/jor.23238. [Epub ahead of print].
3. Holmberg K, Abdolhosseini M, et al. Acta Biomaterialia. 2013; 9(9):8224-8231.
4. Mahato N, Wu X, et al. SpringerPlus. 2016; 5(105) 2010-2015.
5. Costa F, Carvalho I, et al. Acta Biomaterialia. 2011; 7(4):1431-1440.
6. Lindhe J, Meyle J. Journal of Clinical Periodontology. 2008; 35:282-285.