Medical University of Graz

Implantology and histological and macroscopic characterization of rat bones

Summary

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Supervisor:	Prof. Dr. Annelie-Martina Weinberg
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 10, 2020 00:00 and March 30, 2020 23:59 (Europe/Zurich)

Description

Background:

In an interdisciplinary project between the partner institutions BOKU, MUG, TUW and PSI, we are seeking 4 doctoral students to work in collaboration on the multiscale characterization of bone reaction to bio-resorbable implants and the role of mechanical stimuli. This topic is of great medical relevance, since it will not only help to understand the healing process and gradual replacement of the resorbable implant by healthy tissue, but will also reveal the interaction of mechanical stimuli and structure formation, thus potentially opening new insights for therapy. You will get the unique possibility to gain experience in 4 different labs including one of Europe's high end large scale synchrotron facility (Swiss Light Source) at PSI and cut across disciplines in soft matter research.

Bio-resorbable tissue replacements have moved into the focus of research in recent years. Particularly promising candidates for bone implants are magnesium-based alloys, whose biocompatibility and principal suitability as implant material have been demonstrated. Since bone is a complex, highly adaptive material and known to react to mechanical stimuli and chemical influences, implant placement and successive degradation can be expected to alter the bone structure, which is also supported by our preliminary results. Nevertheless a detailed study of the multilevel structural changes of bone during degradation of resorbable implants is still missing. This is of greatest scientific interest because it represents a model system for bone response to a continuously changing healing front and changing load situation. It is also of prime importance for future clinical use of bio-resorbable implants and optimization of medical treatment.

Hypothesis and Objectives:

The main aim of this project is to elucidate the multiscale structural changes in bone caused by a degrading implant and the moving healing front, the correlation of structural changes with changing loading patterns and the consequences for the mechanical performance of bone. We propose to investigate the local morphology and nanostructure in rat bone at the interface to bio-resorbable Mg at different time points during implant degradation. This structural information shall be correlated with the degradation kinetics, healing process and mechanical loading pattern. Varying mechanical stimuli by physical training shall also be considered. Systemic and local biological effects of Mg implants will be evaluated. The impact of physical exercise will be studied in the rat model. Such models will be of high clinical relevance since they offer the scientific basis for purpose-directed large-sample clinical trials and, subsequently, successful patient treatment.

Our work will be guided by the following hypotheses:

1. The continuous implant degradation and bone healing (and therefore continuously shifting bone-implant interface and healing front) cause considerably altered loading patterns that lead to bone adaptation also far from interface.
2. The structural changes are reversible with time as bone is continuously remodeled, eventually leading to a bone structure expected for healthy bone without implant.

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3. Physical training will influence the structure and mechanical stresses at the interface and will support osteogenesis after implantation.

Methodology:

We will use pure Mg, a lean Mg alloying system with very low amounts of Zn and Ca (ZX00). Pure Mg showed higher degradation rates in preliminary experiments than the slow degrading material ZX00. Pure Mg will induce early bone remodeling and fracture healing due to its higher degradation rate and resulting bone turnover and earlier *restitutio ad integrum*. ZX00 will cover the clinically relevant fracture healing case with long-term stability for at least 24 weeks in combination with tight bone contact and low degradation. Both materials showed good bone contact and biocompatibility in preliminary studies. All materials will be dry machined to pin shaped implants, 8 mm in length and 1.6 mm in diameter. Implants will be cleaned with pure ethanol and dried with warm air, followed by sterile packaging and gamma sterilization. 160 male Sprague Dawley® rats will be divided into the following 8 groups: (1) Untreated control without training, (2) Untreated control with treadmill training (TCtrl), (3) sham group without training (SHM), (4) sham group with treadmill training (TSHM), (5) pure Mg without training (MG), (6) pure Mg with treadmill training (TMG), (7) ZX00 without training (BMG) and (8) ZX00 with treadmill training (TBMG). Exercise groups will be selected for treadmill training for two weeks five days per week at different time frames. Animals will sacrificed at different time points. Femoral bones will be harvested, freed from soft tissue and deep frozen for further observations. To investigate changes in systemic bone remodelling markers in rats, we will determine CTX-1, PINP, 25-Hydroxy Vitamin D, TRAP and intact PTH in rat serum at each µCT time point. Additionally, OPG, RANKL and RANK will be also analysed in rat serum. Immunohistochemical assessment will be performed on bones embedded in Technovit 9100 New. Toluidine Blue staining will be used to obtain information concerning general bone morphology. Osteocalcin antibody bone marker will be used in order to detect osteoblasts and, consequently, new bone formation. TRAP staining will be performed to detect osteoclasts and, consequently, bone resorption.

References:

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