Executive Summary

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Project “Porous shape memory scaffolds as mechanically active bone implants“

The aim of this project is the development of smart medical implants that mechanically stimulate the surrounding tissue in a reversible way. In its clinical use these implants act pseudoelastically or absorb shocks and dissipate the mechanical energy during the crystalline transformations between austenite and martensite.

Solid and complex-shaped porous NiTi lattice structures were produced by selective laser melting (SLM) and were physico-chemically characterized. The macro-, micro- and nanostructure (phase transition and crystallographic phases) were investigated. We have demonstrated that the physical properties including the phase transition temperatures can be tailored not only by the composition of the starting powder but also by the SLM processing parameters and by subsequent thermal treatment. The SLM parameters determine the anisotropy, size and arrangement of the grains formed. Mechanically stable implants, which show location-specific damping capacity, pseudoelastic or pseudo-plastic properties, can reproducibly been fabricated.

In cell biological essays with human adult bone marrow-derived mesenchymal stromal cells (hBMSC), the native SLM-NiTi has been identified as cytocompatible material when treated properly. For the investigation of mechanical cell stimulation, a perfused compression bioreactor system (PCB) has been realized. The fully operational PCB allows for programmable stimulation patterns of four scaffolds simultaneously during weeks while monitoring stimulation force and frequency. The custom-made PCB underwent a systematic validation of the cyclic compression regime and the monitoring of the force sensors over a period of five weeks. The force necessary to compress the chondrogenic constructs remained relatively constant throughout the entire culture period. During the loading phase a sinusoidal waveform with a periodicity of approximately 1 second leading to the targeted frequency of ≈1 Hz was determined. Additionally, the PCB has been protected by a European Patent. Cell-biological experiments in the PCB were performed by seeding MSC on collagen-based scaffolds (OPTIMAIX). These soft scaffolds were used in order to accelerate the investigation of the effect of dynamic mechanical loading. These already established collagen-based scaffolds allowed for faster assessments especially in terms of histology. Hypertrophic constructs for non-loaded and loaded constructs after 5 weeks of in vitro culture were characterized. Loaded constructs show a higher degree of maturation as compared to non-loaded constructs. Alizarin red staining of loaded constructs exhibited thicker mineralized borders as compared to non-loaded constructs and mineralized islets were observed within the construct.

As Ni release from NiTi implants may raise concern limiting the applications due to cytotoxicity and hypersensitivity, we investigated the Ni release of SLM-NiTi scaffolds in SBF in loaded and non-loaded conditions. Non-loaded SLM-NiTi constructs show minimal Ni ion release. The mechanically loaded NiTi scaffolds demonstrated a significantly higher Ni ion release within the first 24 h. Thereafter only small, time-dependent increase was detected. The Ni ion concentrations determined in this study remain under the cytotoxic level of 2.35 μg/mL.

The potential for ectopic bone formation in NiTi scaffolds was assessed through ectopic implantation in nude mouse model: The in vivo bone forming capacity of SLM-NiTi reinforced endochondral constructs was assessed. Following an in vitro culture consisting of three weeks of chondrogenesis and two weeks of hypertrophic induction, hypertrophic NiTi constructs were implanted ectopically into nude mice. In vivo bone formation occurred within NiTi scaffolds leading to osseointegration (bone formation along the implant), dense bone matrix formation, and osteocyte formation. The results emphasize the potential of SLM-NiTi as a load-bearing bone implant.

The cytocompatibility and osteogenic potential of SLM NiTi as demonstrated here, along with its superior mechanical properties (i.e. damping, shape memory), highlight the potential of SLM NiTi as a superior bone substitute when compared to today’s Ti implant materials. The

flexibility of the SLM technique, combined with these unique mechanical properties of NiTi, allow for the design of implants better matching the mechanical requirements of a bone repair site than conventional Ti and NiTi implants.