Ni release from rapid prototyped 3D NiTi scaffolds

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INTRODUCTION: The shape memory alloy nickel-titanium is a promising biomaterial for scaffolds and load-bearing implants exhibiting pseudo-elastic or pseudo-plastic behavior allowing for mechanical stimulation of adherent cells and adjacent tissue, thus improving the osseo-integration.[1] For a metal, NiTi has a low elastic modulus, which facilitates the implant design to avoid stress-shielding.[2] However, Ni release from NiTi surfaces and implants still depicts a main concern as its toxic effects have been linked to increased levels of oxidative stress found within cells.[3] With the ultimate goal of fabricating porous implants intended for load-bearing sites, NiTi substrates were fabricated by means of selective laser melting (SLM) and the release of Ni ions as well as the response of mesenchymal stromal cells was studied.

METHODS: Fig. 1 represents a NiTi scaffold 4 mm high and 8 mm in diameter finally built by means of SLM (Realizer 100, SLM-Solutions, Lübeck. Germany) using NiTi powder (Memry GmbH, Weil am Rhein, Germany). Uniaxial dynamic compression on as-received scaffolds mimicking physiological loading conditions along the scaffold's cylinder axis was carried out by means of a servo-hydraulic testing machine (walter+bai AG, Löhningen, Switzerland) with a sinusoidal loading profile, 100 µm displacement amplitude and a frequency of 8 Hz. During the loading cycles, Ni release from NiTi scaffolds was supported via continuous perfusion through the scaffold in axial direction with PBS solution (0.3 ml/min). Samples for Ni release measurements were taken at 24h (691'000 cycles), 1 week ($4.8 \cdot 10^6$ cycles) and 2 week time point ($9.6 \cdot 10^6$ cycles) and the Ni amount was assessed by atom absorption spectroscopy (AAS, Perkin Elmer, AAnalyst 800, graphite furnace, 232 nm).

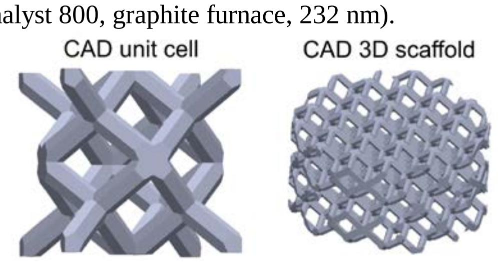

Fig. 1: CAD illustration of the unit cell and the cylindrical SLM-NiTi scaffold (4 mm height and 8 mm diameter).

RESULTS: The AAS measurements reveal Ni release in both loaded and unloaded conditions. The mechanically loaded NiTi scaffolds demonstrate a significantly higher Ni release already within the first 24h. Thereafter only small, time-dependent increases are detected. The levels of released Ni ions are below the cytotoxic level for fibroblastic cells.[4]

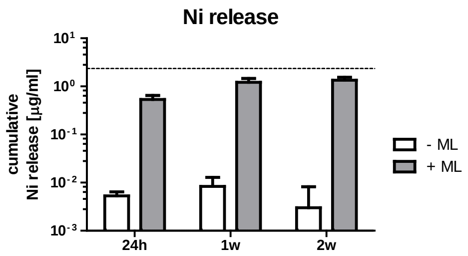

Fig. 2: Cumulative Ni release for unloaded (-ML) and loaded (+ML) NiTi scaffolds. Dashed line depicts cytotoxic Ni ion level[4].

DISCUSSION & CONCLUSIONS: SLM NiTi constructs show minimal Ni ion release if no load is applied. Upon application of physiological loads, cracks may form in the titanium oxide layer on the NiTi surface. Due to the rupture of the protective oxide layer, Ni ions are released into the perfusate and lead to an increase in Ni content. The Ni concentrations determined in this study remain under the cytotoxic level of 2.35 µg/mL[4]. Surface treatments like electro-polishing could further improve the inertness of the NiTi constructs. Moreover, under in vivo conditions, NiTi implants are continuously flushed minimizing local Ni ion concentrations even further. Besides the non-toxic release of Ni ions, mesenchymal stem cells have been shown to colonize NiTi scaffolds and to differentiate along the osteogenic lineage.

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